AUGUST, 1950 Vol. 132 No. 2

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A Monthly Review of Surgical Science and Practice

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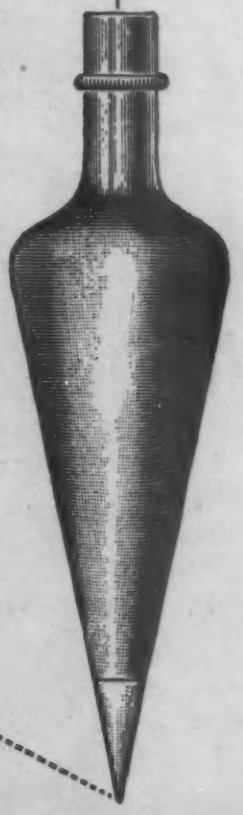

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ANNALS OF SURGERY

VOL. 132 AUGUST, 1950 No. 2

JOHN S. LOCKWOOD

It is with the most profound regret that the Editorial Board and the publishers of the ANNALS OF SURGERY announce the death of John S. Lockwood on Friday, June 16, 1950. Dr. Lockwood's death is a severe loss to the Editorial Board, to the surgical world, and to his wide circle of devoted friends. Dr. Lockwood became an editor of the ANNALS OF SURGERY in July, 1947. His work on the Editorial Board was characterized by enthusiasm, interest and constructive critical judgment. His loss will be keenly felt in the many distinguished positions he held in the field of surgery. He will be missed, above all, as a warm-hearted, generous friend and stimulating companion.

John H. Gibbon, Jr.,
Chairman, Editorial Board

CERVICAL ARTERIOVENOUS ANASTOMOSIS IN TREATMENT OF MENTAL RETARDATION, CONVULSIVE DISORDERS AND CEREBRAL SPASTICITY*

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AN OPERATION DESIGNED to increase the arterial blood supply to the cortex of the cerebrum through production of an arteriovenous anastomosis between one of the carotid arteries and the internal jugular vein, with ligation of the jugular vein proximal to the anastomosis, has been performed successfully in experimental animals and in a few cases in human beings.[1] The procedure was undertaken with the thought that there might be present, in some conditions, viable brain cells enmeshed in a gliotic process and the function of these cells possibly could be improved by increasing the blood supply to the brain. The operation was not difficult. It involved the production of a fistula between the carotid artery and the internal jugular vein. The jugular vein was tied off and cut proximal to the anastomosis, so as to prevent blood from returning directly to the right side of the heart. Arterial blood was thus directed into the brain by both the vein and the artery.

This paper reports the results of the operation in 125 patients.

THEORY

Venous return from the brain has been shown to be asymmetrical. Drainage of blood from the cerebral cortex is usually through the right internal jugular vein and that of the deep portions of the brain is through the left jugular.[2] A significant degree of anastomosis seems to exist between the cortical and deep circulations. Under arterial pressure, a tracer mixture injected retrograde through the right internal jugular vein filled the superior sagittal sinus and all of its visible branches. Material also entered the deep circulation, but not apparently through the Torcular Herophili. The reverse was essentially true upon injection of the left internal jugular vein. Establishment of the arteriovenous anastomosis on the right side should then contribute the majority of blood to the cortex, but significant amounts also to the deep circulation.

Cobb[3] has shown extensive anastomosis to exist among capillaries of the brain. Our findings have confirmed his work and in addition have shown that blood under arterial pressure in the venous system will freely distribute itself throughout the capillary anastomoses. India ink was found in all capil-

* This work was supported in part by grants from the Association for the Aid of Crippled Children and the Cleveland Heart Society. Submitted for publication March, 1950.

laries of dog cortices following such a retrograde right internal jugular injection (Fig. 1). Radioactive iodine, allowed only sufficient circulation time to reach the capillary bed, produced an outline of the vascular tree when tissue sections were exposed to a roentgen ray plate (Fig. 2). Therefore, arterialization of a major venous channel should result in a redistribution of blood flow.

The altered physiology resulting from a cervical arteriovenous anastomosis should not result in undue stress to the cardiovascular system. Arterialization of the venous system has been shown by Beck[4] and Wolff[5] to be fol-

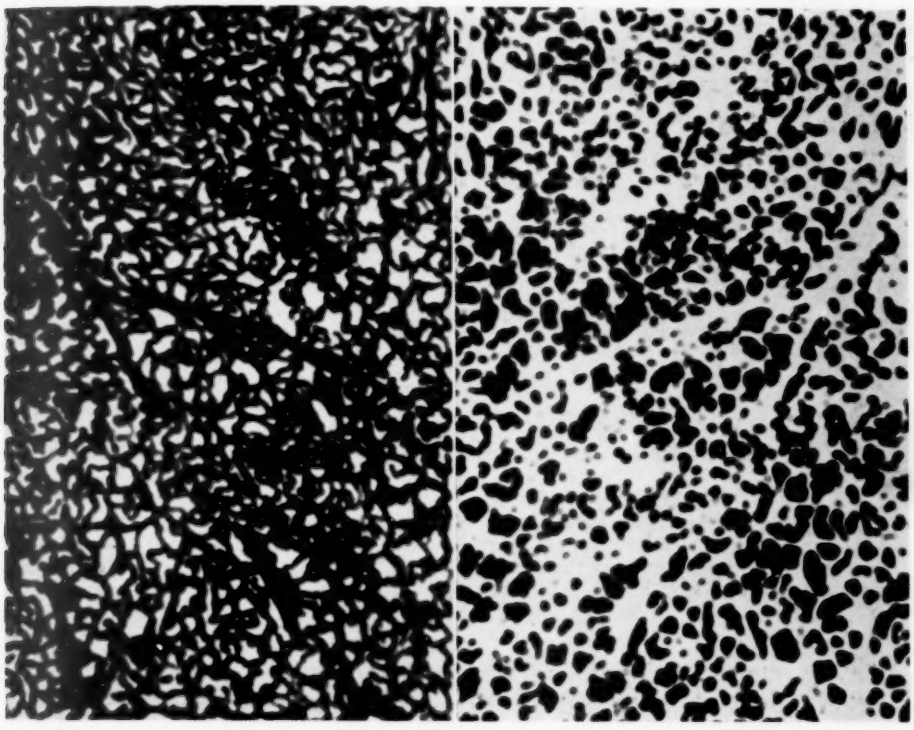

FIG. 1 FIG. 2

FIG. 1.—India ink filling the capillary bed of the cortex following right internal jugular injection under arterial pressure.
FIG. 2.—Radiographic outline of the capillary bed of the cortex following right internal jugular injection of radioactive iodine under arterial pressure.

lowed by hypertrophy of the intima of the veins, thus reducing likelihood of rupture of veins carrying unaccustomed pressures. Cardiac hypertrophy has been known to result from large shunts of blood entering the venous system and returning to the right side of the heart. To reduce the return flow of blood directly to the heart the internal jugular vein is ligated and cut proximal to the fistula and all branches entering the vein up to the base of the skull are ligated. Blood flow to the head or extremities distal to an arterio-

venous fistula may be as much as two or three times normal. Ward and Horton[6] have reported their observation of hypertrophy in the involved part of a large series of such cases. The same hypernutrition, due to increased blood supply with possible opening up of new capillary beds, might result in the brain from cervical arteriovenous anastomosis. A preliminary report on this subject has been made.[1]

Penfield and Erickson[7] have demonstrated a marked deficiency of capillary bed in the periphery as well as in the center of a cerebral scar. The center of the scar is aganglionic, but in the periphery of the zone of gliosis, where ganglion cells are interspersed with glial tissue, there is said to be a deficiency of capillary bed, with continued destruction of ganglion cells in this "intermediate zone" of gliosis. Cells subjected to such hyponutrition might be expected not to function as normally as with the improved blood supply. The drawing in Figure 3 illustrates a normal capillary bed, the plentiful arterioles but deficient capillaries of the periphery of gliosis, and the almost complete absence of finer vessels in the aganglionic area.

FIG. 3.—These drawings of microscopic sections of cortex represent the normal capillary blood supply as compared with the deficiency of the same in the presence of gliosis. The figure on the left represents the normal, while that on the right represents the aganglionic center of the scar. The center drawing illustrates the deficiency of capillary bed in the periphery of the scar.

In an attempt to ascertain the presence of viable but nonfunctioning ganglion cells, in and about the process of gliosis, measurements have been made of cerebral metabolism. Samples of arterial and internal jugular blood were drawn, oxygen content determined, and the arteriovenous oxygen difference computed. The cerebral blood flow as standardized against the determination of Kety and Schmidt[8] established a normal of 72 cc. per 100 Gm. of brain tissue per minute.[1] A series of ten children serving as controls also placed the normal arteriovenous difference at 6.1 volumes per 100 and the normal oxygen consumption at 4.3 cc. per 100 Gm. of brain tissue per minute.[1] A series of 39 children with mental retardation secondary to various types of organic brain injury were studied with the above procedures. Four adults and 22 children with convulsive disorders associated with gliosis were also observed. Since patients with cerebral arteriosclerosis have a pathologic state secondary to reduced cerebral blood flow, measurements in six such patients were also made. For comparison, blood flow and cerebral metabolism

studies were done on five patients with idiopathic or genetic epilepsy. Results within each of these groups are presented in Table I.

Cerebral blood flow is seen to be markedly reduced in patients with organic disease. The children and adults with convulsive disorders had associated mental retardation, and some degree of generalized cortical atrophy was present in all cases. Similar findings were observed in arteriosclerotic patients with senile changes. With the reduction of blood flow in these three groups there was observed an increased arteriovenous oxygen difference, but reduced total oxygen consumption. It would appear that viable cells in the presence of inadequate blood supply may consume more of the total available oxygen than under normal conditions. Compensation, however, may not be sufficient to allow for adequate supply because of the reduced circulation, and therefore the consumption of oxygen per unit weight of brain tissue would be reduced. In contrast to patients with demonstrable organic

TABLE I.—*Cerebral Metabolism in Patients with Marked Gliosis, Arteriosclerosis, or Convulsive Disorders.*

Types of Cases	Cerebral Blood Flow (in cc./100 Gm/minute)	Cerebral (A-V) O_2 (in vols. %)	Cerebral Oxygen Consumption (in cc. of O_2/100 Gm/minute)
Mentally retarded children.....	46.0	7.05	3.2
Children and adults with convulsive disorders with associated gliosis	45.0	6.9	3.3
Arteriosclerosis with senile change	42.0	7.3	3.0
Idiopathic epileptics.....	71.0	6.4	4.2

disease, patients with idiopathic epilepsy did not show a reduction in cerebral blood flow nor an increase in arteriovenous oxygen difference.

These results appeared to support the thesis on which the operative procedure had been developed and gave added justification to further clinical trial.

OPERATIVE PROCEDURE

The operation was done usually on the right side, but it was done on the left side in a few patients. It was recognized that the anastomosis could be taken down if unfavorable results were obtained. It was taken down in 24 patients. The carotid artery was sacrificed in one patient when the anastomosis was taken down. It was preserved in the other patients. More recently the external carotid artery was used rather than the common carotid artery.

The skin incision is made in a transverse direction (Fig. 4). It is placed high in the neck. The incision is about 7 cm. in children and 10 cm. in adults. A vertical incision is made anterior to the sternocleidomastoid muscle. The tissues adjacent to the internal jugular vein are opened. This vein is dissected free up to the jugular foramen. Proper lighting and retraction are necessary to do this. All branches going into the jugular vein are ligated. In about half of the patients the inferior petrosal sinus can be seen emerging through the medial aspect of the jugular foramen. This is occluded with a metal clip. The external carotid artery is dissected free over a segment of artery extend-

ing from the bifurcation of the common carotid artery for a distance of approximately 1.5 to 2 cm. The superior thyroid artery and the lingual artery are seen. The external carotid artery is temporarily occluded above and below (Fig. 5). The internal jugular vein is permanently ligated below and temporarily ligated above. The technic for temporary occlusion consists of an encircling ligature of silk. Both ends of this ligature penetrate a small piece of rubber tube so that when the ligation is made the rubber is included

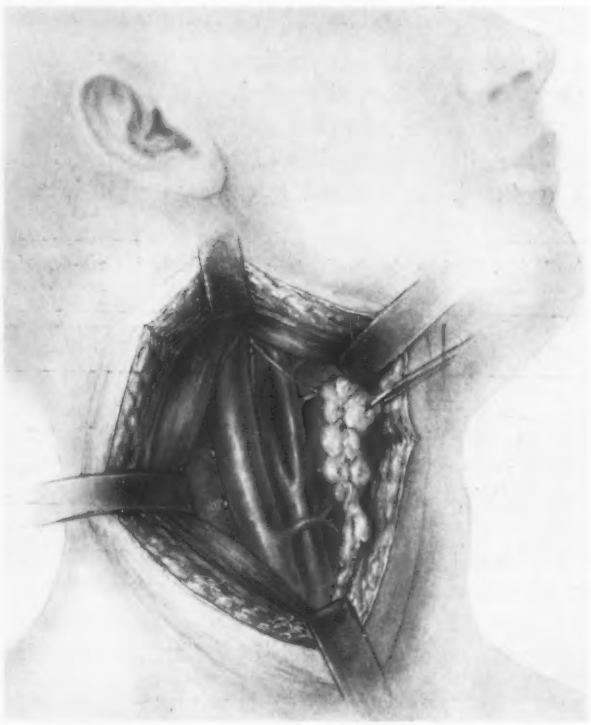

FIG. 4.—A transverse incision is made in the neck. The sternocleidomastoid muscle is retracted. The internal jugular vein and the external carotid artery are exposed. The spinal accessory nerve and the hypoglossal nerve can be seen.

with the vessel in the ligation. The rubber acts as a protection to the vessel. The external carotid artery is incised parallel to the direction of the artery. The linear incision is 3.5 mm. The anastomosis is made by a No. 5-0 Deknatel suture. The suture used is a continuous over-and-over suture. If the fistula is made smaller than 3.5 mm., thrombosis may occur. It would appear that the smaller the stoma the greater the probability of thrombosis. If the fistula is larger than 4.0 or 4.5 mm. then the amount of blood entering the vein may be too great. In this event choked disc, increased intracranial pressure and headache may develop. In two instances the emissary veins dilated and appeared to carry pink blood. The fistula was taken down in these cases.

Swelling of the soft tissues of the eyelids and injection of the conjunctiva were also noted in several patients, in whom the anastomosis was taken down.

In a series of 40 patients in whom the stoma was 3.5 mm. there were two adults and one child in whom revision of the anastomosis was done. If experience in the future indicates that revision of the anastomosis is necessary in a high percentage of patients it may be proper to regard the anastomosis as a temporary procedure, to be taken down later depending upon the course of events.

SELECTION OF CASES

One-hundred twenty-five patients have been subjected to the procedure. Fifty-two children and 26 adults had the original common carotid internal

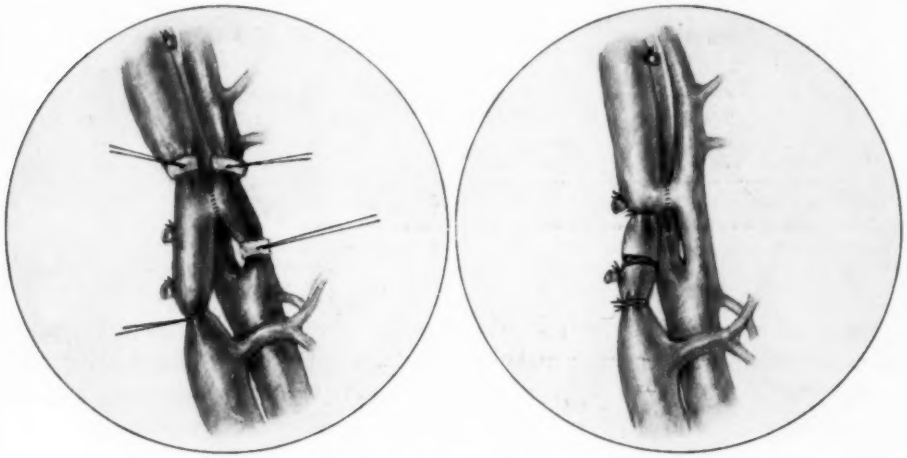

FIG. 5.—Anastomosis between the external carotid artery and the internal jugular vein.

jugular anastomosis; while 41 children and ten adults received the later procedure. Patients selected for surgery were those with mental retardation, convulsive disorders and sensory-motor impairment secondary to brain injury and assumed to have localized or generalized gliosis.

Eighty-nine were children with mental retardation ranging in age from nine months to 14 years. Thirty-four of these children had associated convulsive disorders, and 29 were afflicted with cerebral palsy. Only cases with an obvious diagnosis of birth injury, birth anoxia, encephalitis, post meningitis, post hyperpyrexia, kern icterus, and cortical atrophy secondary to subdural hemorrhage were selected. Developmental anomalies were excluded from the series on the basis of the preceding theoretical considerations. There must necessarily have been normal development with subsequent injury before this operation would have rationale.

There were four adults with convulsive disorders secondary to organic change, and 11 with idiopathic epilepsy. Eight adults with arteriosclerosis and

cerebrovascular complications were included in the series, along with five patients suffering the effects of cerebral emboli and two with thrombosis not secondary to arteriosclerosis. A series of 30 adults with psychoses secondary to arteriosclerosis will serve as the basis of another paper.

The preoperative work-up, especially in the case of the children, included a thorough history. Often an obvious diagnosis of birth injury could be decided on the basis of history alone. The neurologic examination included a lumbar puncture. An electro-encephalogram and pneumo-encephalogram were done both as diagnostic procedures and as reference points for postoperative evaluation. In the children pneumo-encephalography was important in evaluating the diagnosis as well as determining the extent of cortical atrophy. Mild cortical atrophy, as illustrated by the left roentgen ray of Figure 6, supported the diagnosis of moderate generalized brain damage. Extensive atrophy, as seen on the right, served as a contradindication to surgery, because the

TABLE II.—*Range of I. Q. in the 65 Mentally Retarded Children.*

I. Q. Range	10–20	20–30	30–40	40–50	50–60	60–70	70>
Number of children with retardation.....	7	5	15	16	9	10	3
Number of retarded children with convulsive disorders.....	3	2	4	5	3	4	0

large amount of tissue destruction prognosticated little benefit. A marked delta dysrhythmia or a petit mal variant electro-encephalogram dysrhythmia, as illustrated in Figure 7, were usually indicative of cortical damage. Epileptogenic foci were deemed conclusive evidences of cortical damage.

Every case received a psychometric examination, including an evaluation of the intelligence or developmental quotients.

Arteriography has been of value in adult diagnosis in localizing the site of vascular occlusion. It has recently been employed to ascertain the presence of developmental anomalies.

The range of I. Q. of the 89 mentally retarded children is shown in Table II.

RESULTS

The longest follow-up of a patient in this series has been 15 months and the shortest two months. Mentally retarded children were evaluated postoperatively for both objective and subjective improvement. Signs of objective improvement were improved motor function, increased intelligence or developmental quotient, and improved electro-encephalogram. A majority of the patients showed signs of benefit to all observers but could not be classified as having objective improvement and were therefore said to have subjective signs, such as increased "brightness," "alertness," less irritability, improved behavior and greater interest span, greater attention to environment and increased appetite.

FIG. 6.—These roentgen rays represent varying degrees of generalized cortical atrophy. The figure on the left illustrates the more optimal degree of mild atrophy, whereas the marked cortical atrophy on the right is a contraindication to surgery.

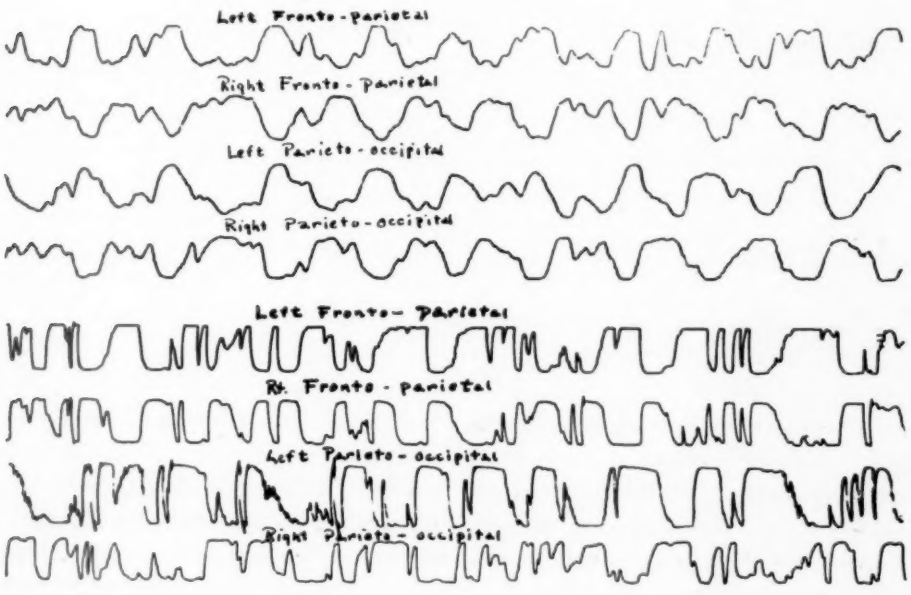

FIG. 7.—Two types of marked cerebral dysrhythmia are shown in this figure. The top four tracings represent marked delta dysrhythmia and the bottom four a petit mal variant dysrhythmia, both of which are often seen with cortical damage.

Children manifesting objective improvement were 35 per cent of the total, while those with subjective evidence were an additional 19 per cent. Forty-six per cent failed to show improvement. Many of the cases showing objective improvement at later evaluations had originally demonstrated only subjective evidence of benefit. These children are classified as to cause and benefit in Table III. With the exception of children with birth injury of various types, the numbers of cases studied fail to represent a significant

TABLE III.—*Eighty-nine Cases of Mental Retardation Classified as to Cause and Benefit.*

Type of Case	% of Total	Number Showing Objective Benefit	Number Showing Subjective Benefit	Number Showing No Improvement
Birth Injury	79.0	26	12	32
Encephalitis	6.0	1	1	3
High Fever	2.0	1	1	..
Post meningitis	3.0	1	1	1
Kern icterus	4.0	1	..	3
Others	6.0	2	1	2
Total per cent	....	35%	19%	46%

series. The three children with kern icterus failed to show benefit. One case of post encephalitic state with a convulsive disorder was improved, three were not.

Within the series of convulsive disorders, our most striking results with children were obtained. Of the 34 cases with organic disorders, five have had a complete absence of attacks, nine have shown complete control with added medication, and six demonstrated improvement with added medication.

TABLE IV.—*Comparison of Results in Organic and Functional Convulsive Disorders Following Surgery.*

Type of Case	Number of Cases	Complete Control	Complete Control With Added Medication	Improvement With Added Medication	No Improvement
Children with organic disorders	34	5	9	6	14
Children with functional disorders	1	..	..	..	1
Adults with organic disorders	4	1	1	..	2
Adults with functional disorders	11	..	..	..	11

Most cases showing complete control had been refractory to preoperative anticonvulsant therapy. One of the four adults with focal seizures has been postoperatively controlled and one has been improved. Two were not helped. Two children with complete control and three children partially helped have had a recurrence of seizures eight to 12 months postoperatively, but to a lesser degree than before. As significant and informative contrast, none of the patients with idiopathic epilepsy have shown postoperative improvement. The results with convulsive disorders are presented in Table IV.

Children with cerebral palsy have been evaluated as having either marked or moderate improvement. Cases with marked benefit have shown decreased muscle tone with resultant improved motor function. Signs of moderate improvement have been decreased muscle tone without motor change. Thirty-one per cent of the cases demonstrated signs of the former and 21 per cent only signs of the latter. The figures were based on findings before physiotherapy. Four cases showing marked change and three with moderate change have shown increased motor benefit following physiotherapy. These children had been refractory to such preoperative treatment. Table V is a tabulation of the results in palsied children.

Four cases of mental retardation in adults over 19 years of age have failed to show benefit.

Change has been observed in half of the adults with arteriosclerosis. In this group we have defined objective benefit as improved motor function,

TABLE V.—*Evaluation of Twenty-nine Cases of Cerebral Palsy in Children with Mental Retardation.*

	Marked Improvement	Moderate Improvement	No Improvement
Number of cases	10	6	13
Per cent of total	31	21	48

return of sensation and improved speech. Difficult to define is the improvement in sensorium and mental acuity. If such is the finding of all observers, the patient is classified as having subjective improvement. A similar standard has also been true of patients with cerebrovascular accidents not secondary to arteriosclerosis. Half of the arteriosclerotics have shown objective benefit and one of eight cases, subjective improvement. Four of eight cases of cerebral vascular accidents not due to arteriosclerosis demonstrated objective benefit.

The postoperative course is usually uneventful and recovery from surgery is rapid. Improvement usually begins to appear in the retarded children within the first two postoperative months. The progress is usually sustained at a persistent rate if improvement is present. In rare cases with objective signs, the I. Q. or D. Q. has risen, then fallen, but never to the preoperative level. Wherever possible, the time rate of improved development is plotted by curve and compared with the preoperative change.

Benefit to adult patients, if occurring at all, has been lasting; however, the complication rate within the older age groups has been much higher than in children.

COMPLICATIONS

In all cases with a patent anastomosis there has been a postoperative rise in cerebrospinal fluid pressure, often to as high as 300 mm. water pressure. The usual pattern is that of a return to normal by the end of the first postoperative week. If increases have persisted for a month, it has been deemed

necessary to reduce the size of the stoma. Three adults with a common carotid jugular anastomosis required such reduction. Only one of 26 children with an external carotid anastomosis has required revision of the stoma size for increased intracranial pressure. He was in the fourth postoperative month and had marked bilateral papilledema. There had been three such cases in children with the common carotid anastomosis, along with six adults with cerebrovascular accidents and five adults with convulsive disorders. Reduction of the size of the stoma in each case proved sufficient to control the symptoms. In two such revised cases there has been a subsequent spontaneous closure of the stoma.

Spontaneous closure had been noted in some early operated cases with a stoma of 2.0 mm. One of these, an adult, has had some return of motor function, whereas preoperatively his improvement was at a standstill. Closure of the anastomosis has occurred in one adult and five children with an exter-

TABLE VI.—*Results in Patients with Cerebrovascular Accidents Secondary to Arteriosclerosis, Embolus Formation, and Cerebral Thrombosis.*

	Objective Improvement	Subjective Improvement	No Improvement
Arteriosclerosis.....	4	1	3
Emboli.....	2	1	3
Thrombosis without arteriosclerosis.....	2	0	0

nal carotid, internal jugular opening. One of the children has been free of convulsive disorders and another has sustained an increase in I. Q. of 15 points in two months. These findings bring up a question whether functional ligation of the jugular vein alone, with resultant redistribution of venous and capillary flow, might be beneficial.

Pulsating exophthalmos is a possible complication of carotid-jugular anastomosis. Exophthalmos is caused by blood in the cavernous sinus under arterial pressure. Postoperatively the pressure in the vein is 20-30 mm. of mercury lower than the artery proximal to the opening. Initially we thought the blood would be under sufficiently lowered pressure so as not to cause this complication. Three children have had exophthalmos, two non-pulsating and one pulsating. One adult had a non-pulsating exophthalmos. None of the patients with an external carotid stoma have had this complication. All previous cases were corrected with reduction in size of the anastomoses.

The possibilities of artificial arteriovenous shunts across the Torcular Herophili, the cavernous sinus and other smaller communications has been seriously considered. Samples of left jugular blood have been repeatedly analyzed for oxygen content to determine the existence of such shunts. On the average, the oxygen content is increased 0.7 volumes per 100 over the preoperative levels. We do not consider this to be a significant rise. Table VII presents these findings in 11 children. In infants with an open fontanel we have been able to obtain oxygen saturation studies on superior sagittal

sinus blood. In five such children the saturation was 16.4 to 18.2 volumes per 100. This is conclusive evidence of the existence of arterially oxygenated blood entering the cortical venous system.

Two mentally retarded children in the seventh and eighth postoperative months developed aneurysms just distal to the site of a 5.0 mm. stoma. For fear of further complication these were closed. One patient has since had a retrogression of intellectual status, but benefit persists in a second case in a child with a convulsive disorder.

Eight children below the age of two years have demonstrated opening of the cranial sutures and return of more rapid skull growth after a closure of several months measured by roentgen ray. There was associated abnormally increased intracranial pressure in only one of the children.

TABLE VII.—*Oxygen Saturation in the Left Jugular Vein Pre- and Postoperatively in Eleven Children with Mental Retardation.*

Case Number	Preoperative O_2 Content In Volumes Per 100	Postoperative O_2 Content In Volumes Per 100
4	9.4	10.1
7	8.6	9.3
11	8.7	9.7
22	9.3	10.2
34	10.1	10.3
37	11.3	11.5
41	9.5	9.9
55	9.4	10.7
56	8.9	9.8
58	10.5	11.4
61	10.7	11.7
Average	9.7	10.4

One patient has had a bilateral common carotid—internal jugular anastomosis without co-existent complication.

The danger of intracerebral hemorrhage, as a result of venous rupture, may not be a remote complication of this procedure. We have no substantial evidence at present that this may or may not be the case. McAllister, Leighninger and Beck[9] have shown the ability of the venous intima to hypertrophy and adapt to high pressure. Wolf had demonstrated the same findings in animals, and Swan[10] in the pulmonary tree of man. These workers have not experienced venous rupture. Johnston,[11] working with revascularization of the extremities, has not had such a complication.

DISCUSSION

Improvement of intelligence in the mentally retarded child is a gradual process, whereas reduction in convulsive disorders and improved motor function are more promptly observed. Dramatic change, in cases of improvement, is also the general rule in adults impaired by cerebrovascular accidents. Some of the latter patients have been up and walking about the wards within two weeks postoperatively. Before surgery, their hemiplegia had prevented such

activity. The original accident had occurred one month to two years before surgery in these cases. Return of articulate speech was observed in two cases.

Many of the patients are free of convulsive disorders during the first few postoperative weeks, but have a gradual return of seizures. Their free interval was probably due to the anesthesia or the pneumo-encephalogram. Some, free of attacks as long as five to six months after surgery, had return of their convulsions. These, and a large number of others have been controlled with added medication, whereas the majority were preoperatively refractory.

A majority of the children showing only subjective improvement by the second or third postoperative month failed to sustain such evidence of benefit. This transient effect may be evidence of only slight potential improvement. A lesser number of such cases went on to show objective signs. The largest number of patients failing to respond to the procedure were those with the most marked retardation and cortical atrophy. The greatest increase in intelligence was observed in the 40 to 60 I. Q. range. Children with an I. Q. above 60 showed less increase in total intelligence but did manifest markedly improved behavior. This was particularly true in two cases of severe behavior problems resistant to psychotherapy.

Genetic or idiopathic epileptics demonstrated no reduction of cerebral blood flow or cerebral metabolism as measured by preoperative study. Theoretically they were not expected to show improvement. Some of the cases with mental deterioration secondary to frequent convulsions did, however, show clearing of the sensorium.

SUMMARY

1. Patients with localized or generalized gliosis of the brain have been shown to have a reduced cerebral blood flow and metabolism.

2. The carotid-jugular anastomosis increases cerebral blood flow and may bring about a revascularization of the brain.

3. Anastomosis between the external carotid artery and the internal jugular vein, within limits of a 3.5-4.0 mm. stoma, has proved to be reasonably safe.

4. About 35 per cent of children with mental retardation, convulsive disorders, cerebral palsy, and a small percentage of adults with cerebrovascular accidents, and other complications secondary to cerebral arteriosclerosis have shown postoperative benefit.

5. The procedure is in the stage of more extensive trial and should be considered as representing a new approach to the problem rather than an acceptable and complete solution.

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CONSIDERATIONS OF BRONCHIOGENIC CARCINOMA*

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IT IS A GREAT PRIVILEGE and honor to be invited to give the Churchill Lecture. You members of the Excelsior Club are to be congratulated on the opportunity which you had to serve under a consultant as wise, able, and understanding as Pete Churchill. Having known him for about a quarter of a century I am not surprised that this club has been organized by this group of devoted admirers to do him honor. He has always stood for the best in surgery, and I can think of no one more suitable for such an honor.

The subject which I have selected to present to you tonight is one which I know has interested him greatly. Despite his great skill and his distinguished accomplishments in other fields of surgery, notably his contributions to our knowledge of the effects of tumors of the parathyroid glands, I believe I am correct in thinking that his true love is chest surgery, a field in which he has been a pioneer, with many splendid achievements to his credit.

Bronchiogenic carcinoma within a comparatively brief period has changed from a subject of curiosity, because of its rarity, to one of very great importance because of its now recognized frequency. In 1912 Adler[1] of New York, who published the first monograph on the subject, could find only 374 cases in an extensive review of the world's literature. In contrast, the condition is now recognized to be one of the most common forms of visceral cancer, and there is some evidence that, at least in male subjects, it may occupy first place, having displaced cancer of the stomach to second place. This evidence consists of two studies. In 1939 Ochsner and DeBakey[2] found at the Charity Hospital, New Orleans, that bronchiogenic carcinoma was the most common visceral cancer. Also, in some unpublished observations, Wheeler recently found over a five-year period that at the St. Louis City Hospital bronchiogenic carcinoma was diagnosed at autopsy more frequently than any other cancer in men. These findings are of great significance, because both hospitals are large public institutions whose patients are residents of their respective communities. Neither institution is in any sense a referral center for patients from a distance with this condition.

Up to the present time there is no satisfactory explanation of the great increase in bronchiogenic carcinoma in recent years. There seems to be no doubt that an actual increase has occurred. Certainly the pathologists of 50 years ago were competent to recognize the lesion at autopsy, and if it was as common then as now there would be no reasonable doubt about it. More

* The Second Churchill Lecture delivered before the Excelsior Club October 17, 1947, at St. Louis. Submitted for publication August, 1949.

probably, it seems to me, during the last 30 years or so there has been some development in our civilization or culture which has produced an exogenous factor responsible for the increase. What this is no one can say definitely at the present time.

Until 1933 the diagnosis of the condition during life was largely an academic question because there was no satisfactory treatment. Now, however, we know that many patients can be cured if a sufficiently radical operation is performed.

In April, 1933, the writer[3] was fortunate in having an ideal patient present himself with a squamous carcinoma involving the bronchus of the left upper lobe. He was a physician, 48 years old. The diagnosis was established by bronchoscopic biopsy made by Dr. M. F. Arbuckle. There were complicating abscesses in the lobe. Despite the fact that I knew of no well-authenticated case of five-year survival after only a lobectomy for carcinoma, it was my intention before the operation to remove only the lobe, partly in order to relieve the patient of the effects of the pulmonary suppuration. At the operation, however, it was found that there was no satisfactory interlobar fissure, and furthermore that all of the tumor could not be removed by a lobectomy. It was decided therefore that the whole lung should be taken out if all the tumor was to be removed, and that it would be desirable to perform the operation in one stage.

Before proceeding with the pneumonectomy some features of the problem had to be considered. No successful operation corresponding to a single-stage pneumonectomy in the human being had been performed previously. Kummell[4] in 1910 removed a lung for cancer, but the patient died on the sixth postoperative day. In 1919 Lilienthal[5] performed a total pneumonectomy for bronchiectasis but the patient died six hours later. Again in 1920 he performed a pneumonectomy in another case, but death occurred 13 days after operation from secondary hemorrhage. In 1920 also, Willy Meyer[6] removed a lung, but the patient died. Nissen's[7] case in 1931 for pulmonary suppuration was of course not a one-stage pneumonectomy, and moreover the patient was a child. In two stages, he passed a ligature around the hilus and the lung later sloughed away. Likewise Haight's[8] case, which was performed in 1932, but not published until April, 1934, was similar to that of Nissen's in that it was a gradual pneumonectomy for bronchiectasis, also in a child. In two stages he ligated the hilus of the left lung and permitted it to slough off. Sauerbruch's[9] case in 1923, a multiple-stage procedure, resulted in the gradual sloughing away of the left lung, and it is doubtful anyway if the entire lung was removed. Macewen's[10] famous case, sometimes quoted as the first pneumonectomy, was probably only a drainage of a very large cavity. From the report in 1906 of his operation, which was performed in 1895, it is clear that he did not remove the entire lung. Archibald's[11] three-stage pneumonectomy in 1932 resulted in death on the fourth day. Windsberg's[12] case, mentioned by Haight as being the first successful pneumonectomy in the United States, was a multiple-stage operation in 1932 for bronchiectasis. Later, how-

ever, the patient died, and at autopsy it was found that the lower lobe had not been removed. It is to the great credit of Windsberg that he reported this later finding. There were, however, numerous experiences of the successful one-stage removal of a lung in experimental animals. In fact I had had some successful results myself. A very excellent review of the literature on the animal experiments has been made by Crafoord.[13] I shall not duplicate it here.

On the basis of the successful animal experiments, I made the decision to undertake the removal of the entire lung, realizing that unless that procedure could be carried out the patient would die anyway from his cancer. I was encouraged to make the decision by the fact that I could not detect any involvement of the hilar lymph glands. The patient, therefore, seemed to be an ideal subject on whom to determine if a cure of a bronchiogenic carcinoma could be obtained by a sufficiently radical operation undertaken before the invasion of the regional lymph glands. Knowing the patient as well as I did I felt even more justified in taking the risk because I was certain that he would rather die of the operation than after a prolonged illness from his cancer.

There was one point, however, which caused me some worry, and that was whether or not the sudden blocking of the left pulmonary artery in a middle-aged man with a relatively normal lung might cause fatal consequences of a kind that follow pulmonary embolism. The only other successful case of the removal of a whole lung, albeit in stages, reported up to that time was that of Nissen, already mentioned. The patient was a 12-year-old girl, who had had a severe crushing injury to the chest previously. It seemed possible that in her case, because of the crushing injury, there might have been gradually produced changes in her pulmonary circulation which would minimize the danger of a sudden ligation of the pulmonary artery. It is true that Sauerbruch had practiced the ligation of the pulmonary artery in a few cases of severe pulmonary suppuration, but here again the conditions were far from normal. Accordingly, I told the anesthetist that I was going to ligate the pulmonary artery, what my fears were, and to observe very carefully the effects on the blood pressure, the color of the patient, the pulse, and the respirations. In order to make the condition easily correctible, I passed a small rubber catheter around the pulmonary artery and tightened it with my hands. Fortunately nothing happened, and I proceeded then with the resection of the lung. A mass transfixion ligature of catgut was used for the hilus, but the pulmonary artery was ligated separately. After the lung was out, the empty pleural space seemed so enormous that seven ribs (the third to the ninth inclusive) were removed in order to accomplish a partial obliteration of it. The immediate postoperative course was uneventful, and on the tenth day the patient, for three hours, attended a meeting of the Clinical Surgical Society which was being held at the Barnes Hospital. Later he developed a small empyema at the upper part of the pleural cavity. The removal of the first and second ribs resulted in the complete obliteration and healing of the cavity.

The examination of the removed lung showed that the carcinoma was only about 1 cm. long but that it was situated almost at the bifurcation of the main bronchus into the bronchus of the upper lobe and that of the lower lobe. Two lymph glands adjacent to the tumor were found invaded, but those removed from the mediastinum were free from any involvement with cancer. The patient seems to have been cured of his cancer, since he is now in his fifteenth postoperative year and he carries on an extremely large obstetrical practice in Pittsburgh.*

The combination of an early case in a relatively young man in good general condition made the circumstances just right for this first successful one-stage pneumonectomy. I happened to be the fortunate one who encountered them. Any other thoracic surgeon who had met with them would have achieved an equally good result.

Since the publication of that case great interest has been aroused in the whole subject of bronchiogenic carcinoma, perhaps because it now seemed possible to apply to a cancer of a lung the same sound surgical principles which had been found effective in the treatment of cancer involving other parts of the body, namely the removal of the entire organ with the lymph glands most likely to be invaded.

Certain questions about the operative attack on the condition immediately arose. Was a thoracoplasty indicated in order to collapse the pleural space, and if so should it be performed immediately or later? Did similar conditions as to operability apply here as to cancer of other organs? In other words, what were upper age limits, did the presence of pleural fluid contraindicate the operation, was a palliative resection of the lung worth undertaking? What was the best method of closing the bronchial stump? These were some of the problems that presented themselves.

Rienhoff[14] deserves most of the credit for showing that a thoracoplasty is not necessary after a pneumonectomy. Except as a means of obliterating an empyema cavity which has developed as a result of a leaking bronchus, a thoracoplasty is not ordinarily performed today.

As experience has developed at the hands of many thoracic surgeons it has been learned that essentially the same principles of operability apply to bronchiogenic carcinoma as to cancer elsewhere except as regards the upper age limit. At least in our experience at the Barnes Hospital, we have found that old patients tolerate the operation of pneumonectomy less well than, for example, the operation for carcinoma of the rectum or the breast. The oldest patient successfully operated upon in our series was 68.† The operative mortality above the age of 60 is considerably higher than that in the preceding decade. Almost all the deaths in the higher age groups are due to circulatory complications, of which coronary thrombosis or infarct is the chief, which may

* Since the delivery of this lecture the patient has completed his sixteenth postoperative year with no evidence of cancer.

† More recently we have successfully performed a total pneumonectomy on a woman 75 years of age.

occur at any time within the first two weeks after operation. The sudden removal of a whole lung, with its attendant disturbance of the pulmonary circulation, seems to be a physiologic blow to an old man of such magnitude that apparently only one with a nearly normal heart can tolerate it.

The presence of pleural fluid, in our opinion, does not necessarily contraindicate a pneumonectomy. The fluid should be examined by aspiration before operation. If it is clear and straw-colored, without the presence of tumor cells, exploration to determine resectability of the lung is indicated. Inflammatory lesions are so commonly associated with bronchiogenic carcinoma that it is not rare to find a pleural exudate which is not due specifically to the cancer. On the other hand, if bloody fluid, or fluid containing tumor cells is found, it is our opinion that a radical operation is futile. Other findings which preclude attempts to resect the lung are (1) evidences of nerve involvement and (2) recognizable metastases. Nerve involvement is evidenced in several ways. First, there is the question of pain. Patients who complain of severe pain have conditions which, in our experience, make a radical resection futile even when it can be done. The pain nearly always means that intercostal nerves or the brachial plexus or both have been invaded by the cancer, and that even if the lung is removed some of the tumor will be left behind in the chest wall. Special nerves which, because of the common location of the tumor, are often involved are the phrenic and, on the left side, the recurrent laryngeal, where it passes under the arch of the aorta. Invasion of a phrenic nerve is readily recognized because of the paralysis of the corresponding half of diaphragm noted on fluoroscopic examination. Likewise, the paralysis of the left vocal cord reveals the involvement of the left recurrent nerve. Rarely, however, it happens, as we have found, that the paralysis of either the diaphragm or the left vocal cord may have been present for a long time due to some other cause. A careful history will be of great help in this connection.

Many methods of suturing the bronchus have been proposed. There is none that is completely satisfactory. Leaks still occur occasionally in spite of the greatest care. Our own preference is two rows of silk sutures, first a row of mattress sutures, then a row of over-and-over interrupted sutures. An additional safeguard to prevent leakage of the bronchial stump is to cover it with a pedicle flap of parietal pleura, which usually can be obtained from the posterior chest wall. Another factor of great importance is the minimizing of infection in the bronchial stump by the liberal use of penicillin (200,000 units) in the pleural cavity immediately after the operation.

The operation of one-stage pneumonectomy is now being performed in all centers where a large amount of chest surgery is done. It has become the standard procedure in the treatment of bronchiogenic carcinoma. It is impossible to know how many of these operations have been performed since 1933. At the Barnes Hospital we have performed 231 one-stage total pneumonectomies, of which 163 have been for tumors of various kinds.* The operative

* Up to March 14, 1949, we had performed 341 one-stage pneumonectomies, of which 226 were for malignant tumors.

mortality, by which is meant deaths before the patients have been discharged from the hospital, has shown a marked decline in recent years. For example, in the year 1947, from January 1 to September 2 we performed 32 pneumonectomies for tumor with two deaths, an operative mortality of 6.2 per cent. The low mortality should serve to remove the idea too prevalent in the medical profession that the operation carries a prohibitive mortality. Similar low mortality rates have doubtless been achieved by other thoracic surgeons.

Of greater interest, however, than the number of patients who survive the operation is the question of how many survive a five-year period. There would be no good reason to subject a patient to such an operation if there were no chance of a five-year cure. Because the operation is so relatively recent I have been unable to find in the literature any statistical reports of five-year survival rates. Some reports of three-year cures have been published, but these are probably of not such great significance as the five-year survivals. I can therefore present only our own figures.

Of 53 patients who had pneumonectomies for malignant tumors prior to 1942, in other words more than five years ago, 15 are alive and well. This is a five-year survival rate of 28 per cent. But in the early years we had an operative mortality of 53 per cent, which means that 28 patients did not survive the operation. In the future, undoubtedly a much higher percentage of five-year survivals will be obtained because of the much lower operative mortality now than formerly. Of the 15 patients alive and well more than five years, three had typical squamous carcinoma, three had undifferentiated lesions, and nine had what we designate as mixed tumors showing invasive features. Some of this last group of tumors might be called adenomas by others and some of them adenocarcinomas. Of the three squamous cell cases, regional lymph nodes were invaded in one, and of the nine mixed tumors regional nodes were involved in five.

I shall not here enter into a general discussion of the pathology of bronchiogenic carcinoma. It seems important, however, to discuss at some length the so-called bronchial adenoma because of a lack of agreement among pathologists and surgeons as to the true nature of this tumor.

The so-called bronchial adenoma nearly always arises in a bronchus sufficiently large to permit bronchoscopic visualization of it. It often produces bronchial obstruction with its attendant complications. Women are slightly more often affected than men, a feature which is in marked contrast to the overwhelming preponderance of squamous bronchiogenic carcinoma in men. Frequently the symptoms suggestive of the adenoma have been present for many years. On bronchoscopic examination it presents itself as a smooth, rounded mass, often pink, projecting into the lumen. Its attachment to the wall of the bronchus is generally by a broad base and sometimes a considerable portion of the tumor is outside the bronchus.

Microscopically the main portion of the tumor is found to consist of cells with scanty cytoplasm and small, round, darkly staining nuclei. The arrangement of the cells is often such as to resemble very closely fetal pulmonary

alveoli, a fact which was first mentioned by Churchill, who reported it as an observation of Bremer of the Department of Anatomy of Harvard.

There is, however, great variation in the microscopic appearance of these tumors. In fact, different parts of the same tumor often present very different arrangements of the characteristic epithelial cells and marked variations in the stroma or mesoblastic elements. An adenoid arrangement of the epithelial cells is commonly so conspicuous that these tumors are sometimes designated by pathologists as adenocarcinomas. In other cases, the tissue of the stroma dominates the picture so that cartilage, fat, smooth muscle, and even bone are seen. Under such circumstances the tumors are frequently called chondroma, lipoma, fibroma, etc. Often they have characteristics so much like those of salivary gland tumors, which are usually designated as "mixed tumors," that in 1938 Womack and I[16] suggested that they be called "mixed tumors of the lung."

The very close resemblance which some of them bear to fetal lung tumors suggests that perhaps they may have their origin in disorganized embryonic bronchial buds which have failed to pursue a normal development. Such a concept is similar to one which Albrecht[17] had many years ago about a tumor of the liver for which he coined the term "hamartoma" from the Greek word "hamartia," which means failure to reach a goal. In 1938 we called attention to the similarity of our concept of the origin of the so-called bronchial adenoma from a disorganized fetal bronchial bud to that of Albrecht for his tumor of the liver. More recently some authors have applied his term of "hamartoma" to these bronchial tumors. The concept implies that for some unknown reason the embryonic bronchial bud has failed to respond to the proper "organizer" and that, after a prolonged dormant period, it has begun again to grow, but this time into an abnormal structure. Such an idea would offer an easy explanation of the occurrence of epithelial elements in such a tumor as the chondroma of the lung (see for example, McDonald, Harrington, and Clagett)[18] and various kinds of mesodermal tissue in the epithelial tumor, or so-called bronchial adenoma.

Of greater importance, however, than the origin of the adenoma is its ultimate fate. There has been an unfortunate lack of agreement on this point. In our article of 1938[16] we advanced the opinion that the tumor is potentially malignant and we reported seven cases out of a larger group in which either invasion of adjacent tissues or involvement of regional lymph nodes had occurred. Kirch,[19] Malkwitz,[20] and von Pein[21] had each previously reported cases of malignant transformations of "adenoma" or "polyp," but little attention was paid to their reports. The opinion which we expressed nine years ago that these tumors are potentially cancerous was not generally accepted and even now there is much skepticism on the part of some pathologists. Let me refer to two rather recent articles. Foster-Carter[22] of the Brompton Hospital in 1941, from a study of 22 cases, states that he has found no evidence of cancer, except perhaps slight invasion of the bronchial wall in a few instances. He says there has never been recorded a case with distant metasta-

sis. More recently (1944) Engelbreth-Holm[23] of the University Institute of Pathological Anatomy of Copenhagen in an article entitled, "Benign Bronchial Adenomas" comes to the conclusion that "in rare cases" the adenoma may undergo malignant transformation, although in all of his 12 cases there was marked invasive growth and in two cases (17 per cent) there were what he considered definite evidences of malignancy. But more cases are constantly turning up in which there is incontrovertible evidence that these tumors may become malignant and give rise to local and distant metastases. In 1942 Adams, Steiner, and Bloch[24] reported five cases under the designation of "Malignant Adenoma of the Lung." In one of their patients there was a metastasis to the vertebral bone marrow; one had metastases to both the mediastinal lymph nodes and to the liver; in another there was involvement of a tracheobronchial lymph node; and in two, the bronchial wall itself was invaded. Anderson[25] of the Department of Pathology of Washington University, has recently reported a case in which there was a metastasis in the liver. Stowell,[26] also of our Department of Pathology, in an unpublished case of an autopsy at the St. Louis County Hospital, has found a metastasis in a regional lymph node.

In a paper presented to the American Association for Thoracic Surgery in 1945 Womack and I[27] reported two cases in which autopsy was performed after bronchoscopic biopsies had established the diagnosis of so-called adenoma. In both cases metastases were found in the liver. In one case the bronchoscopic biopsy had been made four years prior to the death of the patient. There is also the case of Burrell and Negus,[28] unfortunately not reported in satisfactory detail, in which a "fibro-adenoma" had been removed by Mr. Negus through the bronchoscope and "several years after the operation carcinoma of the bronchus developed, and the patient died."

In the discussion of our 1945 paper at the meeting of the American Association for Thoracic Surgery, Bigger[29] cited a case of his in which he performed a pneumonectomy on a man, 48 years old, who had a history of recurring pulmonary hemorrhages for 20 years. The removed lung showed the presence of not only an adenocarcinoma but involvement of the regional lymph nodes as well. Bigger's conclusion was that because of the long history of hemorrhages it seemed likely that the case was an example of a malignant transformation of an adenoma. John Alexander[30] stated that in a series of 13 cases he had had two with lymph node metastasis. In the paper of Chamberlain and Gordon,[31] published in the same issue of the Journal of Thoracic Surgery, a report is made of ten cases of "bronchial adenoma" of which five had lymph node involvement.

Is it necessary to cite more examples to show that the so-called adenoma may undergo malignant transformation?

Those who deny this possibility offer several objections to the idea. First, they say the long history of symptoms often associated with an adenoma indicates that it is not malignant. We do not deny that many of these tumors fail to develop malignant features, but we are convinced that many of them do

undergo a transformation into a malignant tumor and that therefore the potentiality of such a transformation always exists. Furthermore, it is not possible to tell from the microscopic appearance alone whether or not the tumor is already malignant, as many competent pathologists will testify. The bronchoscopic biopsy, therefore, may not be conclusive on this point.

Another argument that is frequently raised is that in a particular individual's experience (as for example, Foster-Carter,[22] Chevalier L. Jackson,[32] and others) he has never seen convincing evidence that the adenoma has undergone a malignant change. Is it not possible that when this change has occurred he has not recognized the finished product as having started as a so-called adenoma?

Let us examine this question further. If we should imagine that a malignant change might occur we might expect that the prevailing type of epithelial cell would be one that is small, round, with scanty cytoplasm, and darkly staining nucleus, in other words the type of cell found in the adenoma. This corresponds very well with the predominating type of cell which is found in two very common kinds of bronchiogenic carcinoma, designated according to orthodox pathologic standards as (1) "round cell" or "oat cell" carcinoma or (2) "undifferentiated cell" carcinoma. Again, the morphologic resemblance of many adenomas to adenocarcinoma has frequently been mentioned, in some cases even by those who deny the potential malignancy of this tumor. Moreover, it seems strange that before the general use of the bronchoscope the adenoma was a very rare tumor in contrast to its comparative frequency now. In his excellent review of the literature, Foster-Carter[22] states that until Kramer[33] in 1930 recognized the first case during life only three cases in all had been described and those were found at necropsy. Even now it is rare to find an adenoma at postmortem examination. Is there not perhaps some explanation of the fact that many are diagnosed during life but few after death? Womack and I venture to suggest that the reason may be that because of the transformation of many of these tumors into carcinomas they are diagnosed as that at the autopsy table and their origin as adenomas is not recognizable.

It has already been mentioned that the so-called adenoma is frequently found associated with other congenital anomalies of the lung. Likewise we[34] have found, in three of nine patients operated upon for congenital cystic disease of the lung, microscopic evidence of abnormal epithelial overgrowth consisting of masses of poorly differentiated epithelial cells having an invasive tendency but showing no metastasis. It seems possible that this condition might go on into the development of unquestionable carcinoma. Also, in another article[35] we have reported four cases of cancer of unclassifiable morphology associated with developmental pulmonary abnormalities of different types. In one of these cases there appeared to be a multicentric origin and the mucosa of the main bronchus presented an appearance, previously mentioned by Lindberg,[36] of many areas suggestive of a precancerous condition. This case likewise seems to suggest that there is no morphologic difference

in cells between bronchiogenic carcinoma arising from the mucosa and that arising from the glandular ducts.

The practical importance of all this discussion on the so-called adenoma concerns the question of its treatment. There is no doubt that many have been successfully removed through the bronchoscope (Jackson,[32] Brock,[37] etc.). Others have been treated successfully with radon seeds (Edwards,[38] Brock[37]). In our opinion, however, they are best treated by radical surgery, either lobectomy or pneumonectomy. One cannot be sure from the bronchoscopic biopsy whether or not the tumor has already become malignant. Again, the bronchoscope will not reveal how much of the tumor is extrabronchial. Finally, extensive bronchiectasis is present so often that radical resection will be required for that reason alone. Although I have performed several lobectomies for the condition, my own preference is for total pneumonectomy. A much better opportunity for the removal of involved lymph nodes is presented in the operation of pneumonectomy than in the less radical lobectomy. Many other surgeons, however, think this recommendation is too radical. Perhaps more experience will disclose that it is.

Improvement in the results of the treatment of bronchiogenic carcinoma will undoubtedly come from the application of the operation of total pneumonectomy to earlier cases. This statement naturally involves the question of diagnosis.

In most cases there are definite symptoms which lead strongly to a suspicion of bronchiogenic carcinoma. These are cough and the expectoration of blood-streaked sputum. When these symptoms are present in a middle-aged man they are so suggestive of bronchiogenic carcinoma that immediate steps should be taken to verify that suspicion. Indeed, one might even say that under such circumstances the burden of proof is on anyone who states that the patient does not have the condition. There are really only two other chronic diseases, with rare exceptions, which are likely to give rise to blood-streaked sputum. These are tuberculosis and bronchiectasis, and the patient is likely to know if he has either one of them.

Further investigation to establish the diagnosis consists of several examinations. A roentgenogram is always of value, but at best it can give only presumptive evidence. The abnormal shadow which is seen is rarely of the tumor itself, but rather of hilar induration and perhaps some atelectasis. Bronchoscopy is of much greater importance because, not only does it often afford an opportunity to visualize the cancer, but at the same time permits obtaining a piece of tissue for biopsy. Moreover, even when the tumor is not visualized, the bronchial washings which may be obtained may reveal cancer cells. Also, to some extent, the question of resectability can be determined by noting whether or not the carina is widened or abnormally fixed and if the growth has extended into the trachea. It is disappointing, however, that in many cases the presence of a cancer cannot be determined by bronchoscopic examination. In our own experience we have been able to make a positive bronchoscopic diagnosis in only 60 per cent of the cases.

The more recently developed procedure of examining the sputum for cancer cells is of very great value. Barrett of England,[39] in 1938 and Wandall of Denmark,[40] in 1944 used this method successfully. The latter author, while in this country in 1945, convinced us at the Barnes Hospital of the great value of the method. The procedure more recently employed by Herbut and Clerf[41] of using the method of Papanicolaou for staining the secretions obtained through the bronchoscope is very helpful. Indeed, the use of the Papanicolaou stain for the examination of the sputum as well as of the bronchial washings is rapidly expanding. This method, however, is not free from danger, since false conclusions, both negative and positive, can be reached unless great care is exercised. The service of one experienced in the recognition of cancer cells is an absolute essential. By means of a combination of roentgen ray, bronchoscopy and cytologic examination of the bronchial washings and sputum we find we can obtain a positive diagnosis in about 75 per cent of the cases of bronchiogenic carcinoma.

What about the remaining 25 per cent? In my opinion the answer to this question is exploratory operation if it seems probable that a reasonable chance exists for a successful pneumonectomy. If the patient is a male of middle age or more who is expectorating blood-streaked sputum, who has a suspicious shadow on the roentgen-ray film, and who does not have active tuberculosis or bronchiectasis, one will nearly always find a bronchiogenic carcinoma at exploratory operation. At least that is our own experience. If the diagnosis is still in doubt after the chest is opened, a frozen section from the suspicious region of the lung will almost always settle the question. In three instances we have removed a lung for supposed cancer when none was present, but in each case there did exist such an amount of chronic infection that the patient was considered to be incurable anyway without its removal. Since each of the patients made an excellent recovery, the procedure can be regarded as having been beneficial rather than harmful to the patient. There is scarcely any need of mentioning the establishment of the diagnosis by the recognition of metastases or by the finding of tumor cells in the pleural fluid; for a patient who has such complications is obviously to be considered as incurable.

One of the most discouraging aspects of the whole problem of bronchiogenic carcinoma is the high percentage of patients who present themselves with a condition too far advanced for a pneumonectomy. In a period of 31 months between January 1, 1945, and August 1, 1947, we have seen 211 cases in which a positive microscopic diagnosis was made. Of this number we were able to carry out a pneumonectomy in only 58 cases, or 27 per cent. In 83 additional cases, or 39 per cent, an exploratory operation was performed, but the cancer was found to be too far advanced to permit the removal of the lung. In 70 cases, or 33 per cent, in which a positive diagnosis was made, not even an exploratory operation was carried out, because the condition was obviously hopeless. Besides these 211 cases of proved bronchiogenic carcinoma there were 49 additional cases in which the clinical evidence

was strong, but no exploratory operation was advised because of the presence of factors such as bad heart disease, too advanced age, etc., which seemed to make unlikely the chance of surviving the operation. It is to be hoped, of course, that as more of the medical profession becomes acquainted with the early features of this condition more patients will reach the surgeon in a curable condition, for bronchiogenic carcinoma is curable if not too far advanced.

SUMMARY

Bronchiogenic carcinoma seems almost certainly to be rapidly increasing. It would seem reasonable to suppose that this increase is due to some as yet unrecognized exogenous factor or factors which have arisen during the last 40 or 50 years.

In about 75 per cent of cases a positive diagnosis can be established before operation. In many of the remainder, when suspicious evidence is present, an exploratory operation should be performed.

The operation of total pneumonectomy is the one which gives the greatest promise of cure. The operative mortality has now reached a respectable rate of less than 10 per cent. In a personal experience, 28 per cent of those patients who had total pneumonectomies were living more than five years after their operations.

The evidence that the so-called bronchial adenoma is a potentially malignant tumor is increasing.

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THE ROLE OF THE ADRENAL CORTEX IN THE POSTOPERATIVE RETENTION OF SALT AND WATER*

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PATIENTS SUBJECTED to major surgical procedures frequently retain significant amounts of infused sodium chloride and glucose solutions in the immediate postoperative period. Cooper, Iob, and Coller[4] found the degree of this retention directly related to the magnitude of the operation. Five of their patients undergoing abdominoperineal resection showed in the first 12 hours after operation a decreased urinary excretion of water, sodium, and chloride, with an increased excretion of potassium. These authors reached no definite conclusions concerning the physiologic mechanism involved in effecting the patterns of water and electrolyte excretion reported in their study.

The influence of the neuro-endocrine system on water and salt metabolism has not been generally appreciated. It has been shown in cats that the pituitary stimulus to the adrenals is initiated within minutes following the onset of stress.[1, 18] Selye[20] has observed in patients an increase in urinary corticoids following injury from mechanical trauma, burns, acute muscular exertion, and acute infections. Any of these conditions may be associated with the suppression of urine.

Corticoids can be fractionated. The physiologic properties of one fraction are similar to, if not identical with, those of desoxycorticosterone which, on administration to human beings acts on the renal tubules to decrease the urinary excretion of water, sodium, and chloride, and to increase the excretion of potassium.[20]

The activity of the adrenal cortex following the trauma of anesthesia and operation, and the relation of this activity to the well recognized postoperative retention of salt and water warranted investigation. Conn[3] had suggested a possible relation in this connection.

In the absence of facilities for the fractionation of urinary corticoids, we selected the total eosinophil count of Thorn and associates[22] as a measure of adrenocortical function. These authors have shown that as adrenocortical function increases the total eosinophil count decreases. While not specific for the corticoid fraction having as its major effect the regulation of salt and water metabolism, this test affords a useful tool for estimating the functional activity of the adrenal cortex postoperatively.

Ten patients have been studied, and in every subject there was a decrease in the total eosinophil count from the preoperative level, the magnitude and

* Submitted for publication February, 1950.

duration of the fall being roughly proportional to the severity of the operation and the duration of anesthesia. Those subjected to gastric or colon resection presented counts that often fell almost to zero within a few hours after operation and not infrequently remained there for 24 hours. This period was characterized by a low urinary volume, an increased rate of excretion of potassium, and a somewhat decreased rate of excretion of sodium and chloride.

PROCEDURE AND METHODS

The patients were unselected except that care was exercised to exclude patients with any evidence of gross cardiovascular or renal disease. Those undergoing colon resection were prepared for operation with oral sulfasuxidine or streptomycin and a high protein, high carbohydrate, low residue diet. Their blood volumes were brought to normal levels with transfusions preoperatively. Serial spinal or a general anesthetic mixture was used for anesthesia. Preoperative medication consisted almost routinely of morphine sulfate 10 mg. and atropine sulfate 0.4 mg. In no subject was there significant hypotension during operation or in the subsequent period of study.

Four patients undergoing colon or gastric operations were weighed on a balance sensitive to 5 Gm. immediately before and after operation. Total body water was measured with D_2O,[11, 12] "extracellular fluid" with sodium thiocyanate,[6] and plasma volume with the Evans blue dye T 1824.[8] The dry sponge technic was used to estimate blood loss throughout the operative procedure, and this loss was replaced as it occurred. While these and additional measurements will be reported later, it can be said here that no dehydration or significant reduction in blood or plasma volume occurred.

In the first seven patients, hereinafter referred to as Group I, 2000 cc. 5 per cent glucose in water and 1000 cc. 5 per cent glucose in 0.85 per cent sodium chloride solution were given in the first 24 hours postoperatively, and this was continued for three days. In two instances it was possible to begin the experiment 24 hours preoperatively, and thus have the patient serve as his own control. In the study of Group I the urinary volume, total output (urine plus gastro-intestinal suction), and total eosinophil counts were measured every 24 hours. The eosinophil counts were done each 12 hours and the two values averaged for the day.

The study of the patients in Group II was set up in such a manner as to duplicate the experiments of Cooper, Iob, and Coller.[4] At the end of the operation the bladder was drained through the indwelling catheter and the urine discarded. Each patient was then given 750 cc. of 5 per cent glucose in water intravenously in each of the first four six-hour periods following operation and rates of excretion of water, sodium, chloride, and potassium were measured. The flame photometer[13] was used for sodium and potassium determinations, and a modification of the Volhard method[9] was employed for chloride analyses. These findings were correlated with the total eosinophil counts taken at the end of each six-hour period.

RESULTS

The results of the first group are summarized in Table I, and the results of the second group in Table II. In Figure 1 are plotted the averages of output and eosinophil counts for the patients in Group I. In Figure 2 are shown the rates of excretion of water, sodium, chloride, and potassium for the patients in Group II.

The preoperative total eosinophil counts per cu. mm. varied considerably in different patients. For this reason the postoperative levels are more con-

TABLE I.—*Five Per Cent Glucose and 0.85 Per Cent Saline, Cumulative Data: Urine Volume, Total Output, and Total Eosinophil Counts.*

	Postop.	Urine ml.	Total Output Urine + Wangensteen Suction—ml.	Eosinophil % Preop. Level
B. B., Male				
Age 69—	1st day	1305	1355	27
Segmental colon resection,	2nd day	2520	2630	45
serial spinal anesthesia	3rd day	730	2690	36
E. G., Female				
Age 66—	1st day	1150	1230	4
Abdominoperineal resection,	2nd day	1755	2375	77
cyclopropane-ether	3rd day	3190	4185	145
A. C., Male				
Age 55	1st day	1160	1310	3
Subtotal gastric resection	2nd day	1075	2175	7
cyclopropane-ether	3rd day	1635	1735	42
M. C., Female				
Age 44	1st day	1180	1440	0
Abdominoperineal resection,	2nd day	4385	4460	61
serial spinal anesthesia	3rd day	2555	2960	200
C. W., Male				
Age 41	1st day	1775	1775	0
Subtotal colectomy,	2nd day	2630	2630	18
cyclopropane-ether	3rd day	2150	2150	28
E. W., Female				
Age 54	1st day	1800	1890	8
Vagotomy cyclopropane-ether	2nd day	2180	2180	67
G. B., Female				
Age 42	1st day	1150	1150	24
Hemorrhoidectomy, spinal	2nd day	2210	2210	124
	3rd day	1910	1910	178

veniently expressed as percentages of the preoperative levels. We formed the distinct clinical impression that the rapidity of the return to normal of the eosinophil count was in some way related to the vitality of the patient. Subjects with advanced cancer seemed to recover more sluggishly following trauma than did the young and vigorous. This requires more extensive observation for confirmation.

The two patients of Group I in whom a 24-hour preoperative control output with the same intravenous therapy was obtained showed immediate large urinary outputs. Yet they, as well as those who received no such preoperative program, presented diminished urinary outputs for the first 24 hours postoperatively. During the second and occasionally the third 24 hours

postoperatively the urinary output increased strikingly. It is to be noted that at the time when urinary output was the smallest the adrenal cortex was functioning most actively, as indicated by the eosinophil curve in Figure 1.

The three patients in Group II showed a decreased excretion of water, sodium, and chloride with an increased excretion of potassium during the early postoperative period. It will be seen that these findings were most marked during the first 12 hours when the eosinophil counts were lowest.

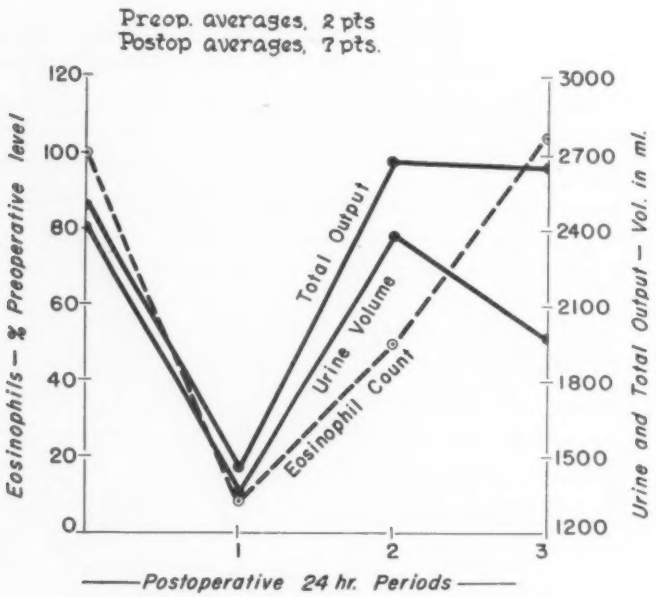

FIG. 1.—Averages of output volumes and total eosinophil counts preoperatively and during the first three days postoperatively. Each patient received daily 2000 ml. of 5 per cent glucose in water and 1000 ml. of 5 per cent glucose in 0.85 per cent saline. Note the similarity of the three curves. The urinary volume and total output (urine plus gastro-intestinal suction) are lowest when adrenocortical function is maximal, as indicated by the profound fall in circulating eosinophils (Data in Table I).

It was found that the volume of gastro-intestinal contents aspirated by Wangensteen suction and the Miller-Abbott tube was usually diminished over the same period, as was the urinary output.

DISCUSSION

In Group I the degree and time relationship of the urinary retention presented a definite correlation with the total eosinophil count. As adrenocortical function increased, as indicated by the decrease in the total eosinophil count, the urinary output decreased; conversely, as the hyperactivity of the adrenal cortex subsided the urinary volume increased.

In Group II it will be noted that there was a selective excretion of potassium and a retention of sodium, chloride, and water in the early postoperative period. These findings agree with those of Cooper, Iob, and Coller,[4] and it is of interest to observe that this type of response is identical with that obtained after the injection of desoxycorticosterone.

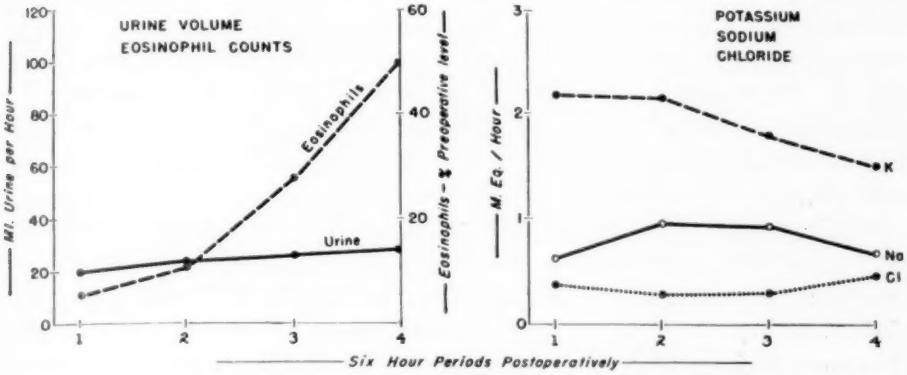

FIG. 2.—Averages of rates of urinary excretion of water, potassium, sodium, and chloride in first four six-hour periods postoperatively. Observe the correlation with the total eosinophil counts. Each patient received intravenously 750 ml. of 5 per cent glucose in water during each of the four periods. (Data in Table II.)

TABLE II.—*Five Per Cent Glucose Administration, Cumulative Data: Total Eosinophil Counts, Urinary Volumes, and Urinary Concentrations of Sodium, Potassium and Chloride.*

		Eosinophils Per cent Preop. Level	Urine Volume ml.	Potassium M. eq/L.	Sodium M. eq/L.	Chloride M.eq/L.
M. S., Male						
Age 68	0–6th hr.	2	100	92.6	20.5	33.5
Abdomino-perineal resection,	6–12th hr.	0	157	85.5	18.1	13.2
cyclopropane-ether	12–18th hr.	10	178	72.5	7.1	7.21
	18–24th hr.	13	171	45.6	4.7	7.83
H. G., Male						
Age 41	0–6th hr.	14	121	125.5	23.9	16.5
Right colon resection,	6–12th hr.	31	146	79.1	29.4	17.5
Serial spinal	12–18th hr.	62	133	54.8	25.9	22.2
	18–24th hr.	78	170	54.8	23.9	39.8
R. B., Male						
Age 37	0–6th hr.	2	142	108.8	55.6	7.59
Gastric resection, spinal	6–12th hr.	2	130	105.8	76.6	6.43
	12–18th hr.	13	148	85.5	83.0	6.81
	18–24th hr.	59	150	67.8	49.0	6.81

There are, however, many other factors which may influence the excretion of salt and water in the postoperative patient.

ANESTHESIA

The effects of anesthesia on renal function have been extensively investigated. Rhoads, Van Slyke, and co-workers[17] in dogs, and Smith and asso-

ciates[21] in man could find no consistent effect of spinal anesthesia on renal excretory efficiency or renal blood flow if blood pressure was maintained. In 1905 Pringle, Maunsell, and Pringle[16] reported the finding that ether anesthesia and operation depressed urine formation. Several years later Hawk[10] studied the renal effects of ether in dogs which were anesthetized from half an hour to four hours and a half. He observed inhibition of urine formation followed by a diuresis of 5 to 25 per cent above normal excretion. Others have in general confirmed the fact that following ether anesthesia, urine output may be depressed for from 24 to 48 hours. MacNider[15] interpreted the physiochemical changes in the blood, in particular the reduction of the alkali reserve, as being directly responsible for the failure of kidney function in the older dogs which he studied.

Cyclopropane was found by Waters and Schmidt[23] to resemble ether in its depression of kidney function. During anesthesia the urine output may be nearly suppressed, but several hours later a compensatory increase occurs. Coller and associates[2] have found inulin clearances depressed and Diodrast clearances variable in patients anesthetized with cyclopropane. These measurements were unaffected by well-controlled ether anesthesia. This group concluded that ether and cyclopropane have no gross effect on glomerular capillary permeability, tubular reabsorptive capacity, tubular permeability, or tubular deaminization of amino acids; that variations in glomerular filtration rate and renal blood flow are probably due largely to "extrarenal" actions of these anesthetics. They further suggested that the disturbances in acid-base equilibrium, body water and ionic distribution, ionic concentration, and cardiovascular function that are associated with disease, anesthesia, and surgery are more likely the causes of postoperative oliguria.

Since our patients having spinal anesthesia without hypotension exhibited the same urinary changes as those who had general anesthesia, it seems likely that extrarenal factors were important in effecting the postoperative retention of salt and water which was observed. Hepatic function tests are affected by anesthesia and operation,[19] and a decreased inactivation of adrenocortical or posterior pituitary extract could conceivably result in deranged water and salt metabolism.

DEHYDRATION

Preoperative depletion of water and electrolytes must be considered, but in our patients this possible criticism was anticipated and the patients were brought to operation in what was considered to be an optimal state of hydration. As mentioned above, the immediate pre- and postoperative weights were almost identical, indicating that the patients had not become dehydrated during the operation. Furthermore, it has been shown that the oliguria in the early postoperative periods following major surgery is unaffected by the additional infusion of blood and/or glucose solution.[4]

NEURO-ENDOCRINE FACTORS

It has become increasingly evident that the regulation of water and electrolyte metabolism is to a considerable extent mediated through the hormones of the adrenal cortex, the two lobes of the pituitary, and the thyroid gland.[5, 7, 14] The adrenal cortex acts in three general ways. First, there is a direct action on renal mechanisms, essentially independent of electrolyte metabolism, the effect of which is to stimulate the rate and extent of water excretion. Second, cortical hormones cause sodium retention by the kidney, the osmotic consequence of which is a retention of water. Increased or decreased diuresis may result from the interaction of these two factors, depending upon the physiologic conditions at the time. Third, there are vaguely defined extrarenal processes by which the cortical hormones affect internal fluid distribution. Such factors appear to involve permeability of phase membranes. All cortical substances studied have a diuretic influence, despite their variable effects on salt excretion, but compound E is a more effective diuretic than desoxycorticosterone acetate. The substances most effective in inducing diuresis are least effective in causing salt retention.[7]

The relation of the adrenal cortex to the posterior pituitary is a complex one. Gaunt, Birnie, and Eversole[7] point out that the anti-diuretic posterior pituitary hormone is secreted at a variable rate and is sensitively responsive to varying states of hydration. At present there is no evidence to show that mild fluctuations in water load alter the rate of cortical hormone secretion. The anterior pituitary also has a role in the regulation of body water, its effect probably being mediated through the thyrotropic hormone which stimulates the formation of thyroxine with its well-known diuretic effect.[14]

The extrarenal effects of adrenocortical function on water and salt metabolism require extensive study before they can be fitted into the general picture, but it may well evolve that effects on phase permeability, the behavior of body electrolytes, and circulatory function are of crucial importance in the ability of the organism to adjust rapidly to the stress of anesthesia and operation.

SUMMARY

A temporary increase in adrenocortical function in response to operative trauma plays a significant role in the postoperative retention of salt and water.

1. The postoperative excretion of urine and certain of its constituents has been correlated with adrenocortical function, as indicated by the total eosinophil count.

2. Infusions of 2000 ml. of 5 per cent glucose in water and 1000 ml. of 5 per cent glucose in 0.85 per cent saline were administered daily for three days following operation in five patients who had undergone partial colon resection, one a vagotomy and one a hemorrhoidectomy. The urinary volumes and total outputs (urine plus gastro-intestinal suction) were correlated

with the total eosinophil counts. It was found that the curves could be almost superimposed.

3. In a second group of three patients, one of whom underwent gastric resection, one resection of the right colon, and one a combined abdominoperineal resection, 750 ml. of 5 per cent glucose in water were administered in each of the first four six-hour periods postoperatively, and rates of urinary excretion of water, sodium, potassium, and chloride were measured and correlated with the total eosinophil counts in each period. When adrenocortical function was maximal, as indicated by a profound fall in the total eosinophil count, these patients exhibited a decreased rate of excretion of sodium, water, and chloride with an increased rate of excretion of potassium. The rates of excretion confirm the work of others, and are identical with the results obtained following the administration of desoxycorticosterone.

4. A number of factors which might affect the postoperative excretion of salt and water are discussed.

5. The clinical impression was gained that the vigor of eosinophil response to trauma may be in some way related to the vitality of the patient.

6. Attention is drawn to the diminished volume of fluids secreted into the intestinal tract during the first 24 hours postoperatively. This may represent but another manifestation of profound generalized derangements in membrane permeability. This finding is being further investigated.

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COMPLETE SCALP AVULSION: RATIONAL TREATMENT

REPORT OF CASES; EXPERIMENTAL BASIS FOR PRODUCTION OF FREE, HAIR BEARING GRAFTS FROM AVULSED SCALP ITSELF*

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SCALP AVULSION is an injury which has far-reaching effects upon the patient out of all proportion to the minor disturbance of essential body functions entailed. Fatalities in reported cases have been almost unknown in recent decades, but the injury, if uncomplicated by other traumata, as it usually occurs, has serious consequence in terms of length of hospitalization, economic loss to the patient and to the community, and, most important, in the devastating disfigurement and psychologic effects of this which the patient endures after the reconstruction is completed. John Staige Davis,[2] in 1911 reviewed the subject up to that time, adding many cases collected from his colleagues, and outlined principles of treatment which have been improved little since. Kazanjian and Webster[6] reported their experiences with the problem in 1946, reviewed the literature, and emphasized that the ideal time to apply grafts for reconstruction is immediately, and that, *pari passu*, freshly denuded pericranium is sufficiently well vascularized to bear split skin grafts very well.

The case reported herein was treated with immediate application of superficial split grafts taken with the Padgett dermatome from the avulsed scalp. Taking such "Thiersch" grafts or dermatome grafts has been recommended by almost every author who has written in the English literature since it was suggested by McWilliams in 1924.[7] Apparently, all have been unaware that this had been recommended in 1920 by Geinitz[4] and actually employed and reported by Eckhardt[3] in 1939. Geinitz reported an experience with four cases, treated with variable success with immediate application of split grafts taken from the thighs. He offered detailed recommendations about tacking an avulsed scalp to the wooden head of a milliner's mannikin and cutting Thiersch grafts from it with a razor type of grafting knife. Eckhardt employed the method with great success when an extensive avulsion was completely reconstructed in six weeks (!) by combining grafts from the scalp with additional ones from the thighs. As has been true with our patient, his patient grew no hair from the scalp grafts.

Most extensive scalp avulsions in the recent (and most American) literature are incurred by female factory workers whose hair is caught in fast

* This study was made possible by a grant from the Sias Research Laboratory, Brooks Hospital, Brookline, Mass., and the assistance of Dr. Howard Lind, Director, and his staff is gratefully acknowledged. Submitted for publication July, 1949.

moving conveyor belt mechanisms, rollers, or other insufficiently guarded machines. Cases reported in the European literature two and three decades ago relate injuries sustained with threshing machines in use in fields—women working with then unfamiliar hazards. There are recorded accounts of the scalpings practiced by aboriginal warriors of centuries gone by, and of the problems which beset the physicians who attempted to aid victims of scalping who survived the event. A fascinating account was recorded by Strayer;[11] he relates the experience of Augustin Belloste, who made small perforations in the outer table at the first dressing of the wound to prevent bone necrosis—this in 1696.

Case 1.—(Brooks Hospital No. 1827.) P. C., a 17-year-old, single, white, candy factory stapling machine operator was admitted to the Brooks Hospital on July 15, 1947, 30 minutes after sustaining an injury in which her hair was caught in a moving conveyor belt system with resulting complete avulsion of a large part of the scalp. There had been no loss of consciousness or associated injury. She complained of only slight pain around the site of injury. Past and family histories were not contributory.

Physical Examination. The patient was a pale, moderately obese, well-developed and nourished young white female in slight distress. Blood pressure 130/70, pulse 68, normal sinus rhythm. Remainder of examination was essentially normal and non-contributory except for the head. There was complete absence of approximately 70 per cent of the hair bearing skin of the head; this was cleanly avulsed from an area bounded anteriorly by the hair line across the forehead, obliquely down the left parieto-occipital region to a point below and posterior to the external auditory meatus, posteriorly on the right at a slightly higher level, the posterior boundary lying just cephalad to the occipital protuberance (see Figs. 2 and 3). The wound edges were only slightly irregular and gave the impression of having been made with a fairly sharp cutting instrument; there was little bleeding. The base of the wound was grossly clean, and slightly edematous periosteum containing dilated small blood vessels was intact; this tissue later showed a pink blush when small vessels continued to dilate. Scattered punctate areas which bled dropwise were noted (see Fig. 1 for typical appearance of a fresh scalp avulsion with periosteum intact). The avulsed scalp itself, which was sent for and received as soon as the patient's status had been appraised, was in 4 fairly cleanly divided pieces with regular edges measuring 10 cm. on each side; their deep surfaces bore the smooth, glistening galea aponeurotica which indicated the usual sub-galeal avulsion. The superficial surfaces bore long blond hair.

Laboratory Examinations. Urine essentially normal; hemoglobin 10.9 Gm. per 100 cc., erythrocytes 3.93 million per cu. mm.; leukocytes 10,250 per cu. mm.; blood smear normal; fasting blood sugar 108 mg. per 100 cc.; non-protein nitrogen 46 mg. per 100 cc. (later 38); blood Hinton reaction negative. Roentgenograms (taken while operating room was being prepared) showed no skull fracture.

Course. The patient was immediately given Demerol, 100 mg. subcutaneously; the head was enclosed in sterile towels, and intravenous 5 per cent dextrose in saline infusion was started. She received 500 cc. of citrated whole blood during the first operation, and additional similar transfusions on the evening of this and two succeeding days. The anemia was then fully corrected and did not recur. She received daily dietary supplements of ferrous sulfate (900 mg.) as well as vitamin B complex and vitamin C. Penicillin in 100,000 units every 4 hours and 4 Gm. of sodium sulfadiazine (given intravenously, later orally, with maintenance of a measured blood level between 4 and 10 mg. per 100 cc. on one Gm. every 4 hours) were started and continued for 2 weeks, given thereafter for 2 days before and one week after successive skin grafts.

In the operating room, using aseptic technic with changes of gowns, gloves, and instruments between the stages described, the pieces of avulsed scalp were shaved cleanly

free from hair with a razor blade held in a hemostat, and were cleaned with sapo mollis solution, 70 per cent ethyl alcohol, and ether. The pieces of scalp had been placed in a sterile basin of isotonic saline solution covered by sterile towels and kept over a pan of cracked ice in a refrigerator. After shaving, the pieces were again returned to a basin of cold saline solution. The patient's head was shaved around the wound margins and with the open wound protected by sterile sponges the edges were cleansed with sapo mollis, alcohol and ether. The open wound was exposed and a few loose hairs present were picked out, the whole then being irrigated with warm saline solution. No anesthesia was required for this or for subsequent suturing; the patient complained only of a slight stinging sensation around the wound margins. The superficial surfaces of the scalp pieces were then singly wiped dry and coated thinly with the commercial "Padgett Dermatome Cement" as was the drum of the dermatome; the pieces were glued to the dermatome drum and with the blade set according to the calibrated scale, after previous adjustment to zero, superficial grafts were cut from each piece with thicknesses ranging from .015 to .050 inches. An effort was made to secure thin grafts, but because of the novelty of the method (to us) and certain technical difficulties the grafts were finally taken as described. Two of the pieces which had slightly irregular shapes were bisected before cutting in order to secure a better fit on the dermatome drum. Technical details made this procedure a tedious one; these are easily learned as will be discussed. The 6 grafts thus secured were sutured in place with interrupted fine black silk sutures so as to cover 90 per cent of the denuded cranium. The scalp edges retracted away from the wound quite readily, and the defect requiring coverage was decreased in size by 2 cm. (measured along each radius) by suturing these edges to the fibrous pericranium; the graft sections were sutured to one another but were also anchored occasionally to this periosteum. Parresine gauze (wax impregnated wide mesh gauze) was then applied beneath fluffed surgical sponges and a snug head bandage; over this, strips of "Elastoplast" bandage (an elastic cotton bandage bearing an adhesive substance on one surface) were placed in an effort to secure the best possible even pressure over the entire area. The procedure was well tolerated.

On the seventh day, after suitable skin testing, the patient was given 1500 units of tetanus antitoxin serum; the administration of this was deferred until it was thought to be less hazardous for the skin grafts if there should be any generalized cutaneous reaction. On the ninth day, with sterile technic, the first dressing was performed and photographs were made (see Fig. 2). There was viability of the grafts, with loss of two sections cut at .040 and .050 inches, the thickest ones, and the final percentage of "take" was estimated at 70. Sutures were removed and dressings of parresine gauze and moist (saline) sponges were applied; "Ace" bandages were helpful in these dressings. They were changed daily, and mechanical debridement aided in securing clean areas free of slough of grafts which were not viable.

Before the next grafting (on the thirty-first hospital day) "air dressing" was essayed with a plaster of Paris jacket enclosing all of the head except the face and scalp areas under consideration, wire struts (made from bent sections of coat hanger wires) protecting the wound from contact with bed clothes, etc., the whole covered with gauze bandage over the wires. This was well tolerated (it was in essence the "Minerva jacket" used by orthopedists), but it was soon apparent that it was not needed, and that the field was sufficiently clean to allow further grafting. The usual benefit of air dressing was noted, with no exuberant growth of granulation tissue in a field which remained quite clean and free from exudate.

On the thirty-first hospital day, using local one per cent procaine hydrochloride with 1/50,000 adrenalin to block the lateral femoral cutaneous nerve and the skin intra- and subcutaneously just across the upper border of the donor sites, half dermatome drums of skin were taken (.015 inches) from right and left lateral thighs. After dressing of the donor sites, the head dressings were removed and after complete change of instruments, etc., the grafts were cut to shape and sutured in place with interrupted No. 36 stainless steel wire. Most of the still denuded pericranium was thus covered; it was noted then and later

FIG. 1

FIG. 2

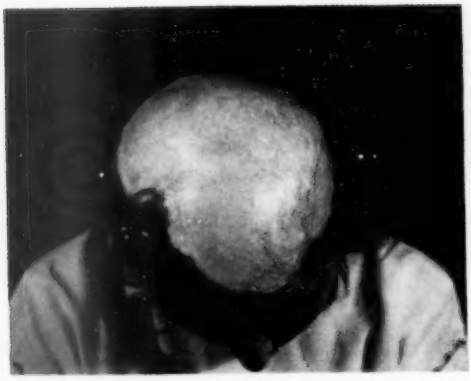

FIG. 3

FIG. 4

FIG. 1.—Typical appearance of patient immediately after avulsion of scalp leaving intact pericranium. This patient is not the one described herein or pictured in Figures 2 and 3. Appearance of both wounds was the same except for extent; note punctate hemorrhage and diffuse blush.

FIG. 2.—P. C., Brooks Hospital No. 1827, first dressing, nine days after injury; viable and non-viable grafts are present.

FIG. 3.—P. C., fourteen months after injury; note absence of atrophied skin or prominent scar tissue.

FIG. 4.—Re-splitting of pig skin .040 inch graft left on dermatome drum. The instrument is now set at .015 and thus a graft indicated as ½BCD is being formed. The layer A½B, .015 in. thick, remaining on the dermatome drum will be discarded.

that there was slow but continuous retraction of the wound margins until healing was complete; the areas requiring grafting were therefore more extensive than would have been supposed at the time of original injury. These grafts measured about 8 cm. on each side; they were dressed in the fashion of the first grafts, and 7 days later were found to be about 80 per cent viable. Inasmuch as the recipient sites were almost ideal, with flat, thin beds of clean, pink granulations, and 100 per cent viability of grafts could be anticipated, failure to achieve this here or with the original grafts seems to have been due to the inherent problem of immobilization; it was to solve this that the plaster jacket had been tried (in part). Having the patient sleep in a semi-sitting position, sleep without pillows, etc., were also evaluated. A really satisfactory solution was not found, and a head dressing which is not too bulky and is firmly applied with elastic adhesive bandages best seems to immobilize with firm, even pressure. Careful bacteriologic control with smears and cultures made in the intervals between grafts demonstrated a variety of saprophytic and non-virulent organisms. There were no streptococci identified, nor was there ever evidence of any true virulent local infection or invasive cellulitis or lymphangitis. The temperature chart remained flat except at the time of a mild upper respiratory infection.

On the fifty-third day another small dermatome graft was applied in similar fashion, with complete "take" and on the seventy-fifth day, after the patient had been allowed to go home for a few days, 2 small (1.5 cm.) areas were covered with razor grafts cut very thin. The patient was discharged completely healed after a wig had been secured for her on the eighty-second day after injury. The original hair had been saved, but contrary to the usual published experience, the prosthesis makers consulted felt that a better transformation could be made without using this.

The patient has been followed and noted to have smoothly healed skin without atrophy, scar between graft sites, or subjective complaints. The grafted skin and all lines of juncture are freely movable. There has been return of sensation of light touch, but not heat, cold or pain, around the periphery over a one centimeter area. The thicker grafts used bear some fairly dense, very fine (almost invisible) hair which is easily broken off. There is a small (0.3 cm.) nodule which has the appearance and consistency of an epidermal inclusion cyst between two of the grafts. The patient has become seclusive, has not returned to work, and anxiously awaits further reconstruction. She usually wears a turban in preference to the wig, and the long hair which has grown around the site of injury allows a semblance of normality. Further reconstruction employing the new principle described below, or using pedicle flaps of the remaining hair bearing skin (to advance the hair bearing portions to the front and sides of the head), will be undertaken shortly (Fig. 3).

PRINCIPLES AND PROBLEMS

The temptation to replace an avulsed scalp in its original form is great. However, there are nearly 100 reported cases where this has been tried, with universal failure, and it seems important that its impossibility be better known. It has been attempted as often in recent years as before (usually by those not well versed in principles of traumatic and plastic surgery). As Straith[10] says, few surgeons have the opportunity to treat more than one such injury; patients are seen by skilled plastic or general surgeons after this attempt has been made and has failed. However, knowledge of the working of any calibrated skin grafting device and an appreciation of the principles which apply are all that is needed to achieve good results.

The usual scalp avulsion carries away all layers down to and including the galea aponeurotica, leaving pericranium, the periosteum of the outer table of

the skull, which derives its blood supply from the diploic circulation with small vessels which penetrate the outer table. The major vessels which supply the scalp are interrupted as they traverse the fatty areolar layer of the scalp superficial to the galea. Tearing tends to occur through the thin skin anterior to the scalp across the forehead, often with loss of the eyebrows and all skin of the forehead; it has been suggested that the supraorbital ridges serve as blunted knives or levers over which tearing takes place. Occasionally the upper portions of the ears may be lost, the external auditory meatus being the site of strong and fixed connections. Posteriorly, variable amounts of suboccipital skin of the neck remain. Undoubtedly the speed, violence, and direction of the trauma determine the boundaries of avulsion; special problems of reconstruction are posed when portions of ears are missing, or when fibrosis and contracture deforms the shape and interferes with function of the eyelids. Hair alone is rarely avulsed in any extensive injury (Kazanjian and Webster found only one report of such an event[6]). Small avulsions which can be closed primarily with flaps of intact scalp should be so treated, since that method (along with replacement of any avulsed scalp attached by an appreciable pedicle, however small) is notably successful because of the extensive blood supply which the scalp enjoys. Galea is recognized on the undersurface of the scalp as a smooth, glistening, firmly fixed (to the scalp) sheet of tissue. Intact pericranium may be visualized as a cover of typical periosteum; it bears many small blood vessels which become dilated with the passage of time after injury, and may be transfixed with a curved needle for placing sutures (Fig. 1). The galeal layer may, in part, be left behind in avulsions, and the scalp torn away will then present a layer of fatty tissue in which hair follicles can be seen on the deep side. In the event that this is the level of avulsion, primary grafting may be expected to succeed easily because of the remaining vascular connections with the major blood supply of the scalp.

In the event that pericranium is also absent, or if it is absent from any part of the field, this must be recognized and management varied accordingly. Despite statements to the contrary which have appeared in the literature, "bare bone" will not support free skin grafts, and what has too often been referred to as bare bone has clearly been bone devoid of all tissues *except* periosteum. Our experiences in the treatment of compounded fractures of the long bones with loss of soft tissue at the Boston City Hospital have repeatedly demonstrated that thin (and occasionally thick) split skin grafts will do well in a sufficiently clean, freshly incised field over intact periosteum, but fail when placed over completely denuded cortical bone unless the denuded area is very small. They will grow if the cortical bone is immediately cut away and grafts can be placed and firmly held over freshly exposed cancellous (medullary) bone. These are important considerations, and too many reported cases have demonstrated failure of early grafts and gone on to necrosis and sloughing of an exposed tabulla externa of the skull. The situation improved when multiple drilling through the outer table was employed, preferably immediately (as was

recommended in 1696 by Belloste[11]), although even this has not always prevented sequestration and bone slough between the drill holes; the goal of this maneuver has been to secure growth of granulations up from the diploe and over the denuded bone. When employed, there is loss of the golden opportunity for good healing which the clean wound presents, to say nothing of loss of the chance to use the avulsed scalp itself as a source of grafts. Drilling the countless holes needed has been a long and tedious procedure, and, as first suggested by Geinitz[4] and later reaffirmed and actually used by Kazanjian and Webster,[6] shaving away the outer table with a sharp chisel or osteotome is better. To this may be added the immediate application of grafts over the cancellous bone thus exposed. Hemostasis in the field of freshly denuded cancellous bone can be achieved with the passage of time aided by application of dry or cold saline sponges; the use of bone wax, topical application of thrombin, fibrin foam, oxycel, gelfoam, etc., seems quite illogical here, where additional clot or foreign body would be interposed between the grafts and their sources of blood supply. Thus, denudation of the skull of periosteum must be recognized and treated appropriately, but need be no bar to immediate skin grafting. Attempts to preserve the avulsed scalp for later use by refrigeration methods (which have been reported in some detail[12, 13]) are unnecessary and uncertain.

Other pertinent principles and technics warrant description. The avulsed scalp must be secured if it is to be used, and cooling of it and any grafts taken will contribute to ultimate viability. Heat increases the rate of metabolic processes, which must be continuous, and grafts are endangered by the hours between injury and resupply from recipient sites. Drying must be avoided. However gross the initial contamination may be, after mechanical cleansing and aseptic handling, grafts cut from an avulsed scalp will be relatively sterile because the surface to be applied to the recipient site has been completely buried in intact tissue until cutting is done. Antiseptics should be kept away from tissues to be used as grafts as well as from recipient sites. The author believes that rapid correction of anemia with blood transfusions is most important. Antibacterial agents, as penicillin, sulfonamide preparations, etc., probably prevent invasive local infection which can be so devastating to a skin graft, but these infections were uncommon causes of failure before the advent of the newer agents, and the agents themselves have brought about no revolution in the procedures possible in reconstructive surgery. At best they allow only partial relaxation of rigid bacteriologic control in handling open wounds. For anesthesia we greatly prefer local use of procaine with nerve blocks where indicated (as in taking dermatome grafts from the thigh); Pitkin's descriptions of these technics are invaluable.[9] A great advantage in plastic surgery of the head and neck is the complete co-operation of a conscious patient in applying drapes and dressings (without the hazard to sterility of the field of the anesthesiologist's hands, mask, etc.) and in positioning the parts involved during operation. For suture material we prefer very fine stain-

less steel wire, which carries no infection into the depths of the wound by capillary action, and about which very thin skin grafts heal without ulceration around each suture. Retraction of scalp edges is a problem only partly solved by suturing them to pericranium; it is desirable to use any slack to make the defect smaller and to avoid late retraction if the primary reconstruction is not complete. Our experience with periosteal suture and with plaster encasement (to which sutures might be attached to hold the scalp edges) was disappointing.*

* The method of producing dermatome grafts from free pieces of skin or scalp deserves mention. The method used in the experiments described below is a modification of that described by Zintel[15] for increasing the yield of graft skin from limited donor sites—forming "split-split" grafts. Free pieces of skin, after surface drying, are thinly coated with a layer of adhesive substance and applied to a similarly coated dermatome drum face. Only the epidermal side can be so used, as the small amounts of fat present after any thin graft is removed destroys the adherence of the cements. Drying of the cement is slow on cooled skin (or donor site in Mock's refrigeration anesthesia[8]) and is facilitated by using a very thin coat and by the aid of the air stream from an electric fan. Conversely, a warm, recently autoclaved dermatome drum causes the cement to boil, so that small bubbles formed present difficulty. We have found that ordinary stationer's rubber cements (made with low boiling petroleum ethers and naphtha as solvents for latex and resin preparations) are superior to the commonly offered ethyl ether solutions. The rubber cements dry rapidly, and sudden disappearance of their penetrating odor over the field in question is good indication that they are ready for use. Should any thick spots occur, a light touch with the finger tip will unroof these and allow deeper drying. Cement once applied must be allowed to dry or be entirely reapplied—no patching should be attempted. If the free piece of skin is to be stretched, this must be done before coating with cement, or the integrity of the coat will be disrupted. It has been our experience that as long as there are no gross wrinkles, stretching is unnecessary and it requires extra hands. Operators should remember that the final effective thickness of any dermatome graft varies with stretching (or the lack of it) of the skin used as well as with the degree of tension applied to the graft when it is sutured in place. The character of skin grafts which allows stretching makes them fit well and accommodate themselves to most irregular shapes. It is important that cement be applied up to the very edge of free pieces of skin, which may then be placed on the drum of the previously prepared and adjusted dermatome. Once applied, even pressure suffices to cause firm adherence, and care should be taken not to disturb the adhesion between the coated surfaces by ill-advised attempts to repair faulty preparations with increased pressure. The calibrated blade may then be set for whatever depth is desired for the deepest cut. Use of the calibration system of the dermatome is preferred over setting the blade with visual control using the two lateral adjustment screws, as is often done. It must be granted that a dermatome which is worn and has a loose axle (identified by a rattling sound when the instrument is shaken) will usually cut from .005 to .015 in. deeper than the setting, but the error is systematic and will occur however the instrument is set. Failure to use the calibrated scale simply deprives the operator of an accurate and reproducible measure of graft thickness, and he should account for the increased thickness which the instrument may cut in any event.

The initial cutting may then be made; an assistant's observation of the lateral edges of the skin piece on the drum is helpful. If there is rolling away from the drum, it can be prevented before serious damage is done by light pressure from the assistant's finger tips at the very edges maintained just in front of the moving blade. By this means, a superficial graft is cut from a free piece of skin or scalp; this was the method (with certain improvements) employed in the case reported. The author has used this technic in securing

FREE HAIR BEARING SKIN GRAFTS

Hair-bearing properties of free grafts of different thicknesses taken from varying depths in the skin of young pigs were investigated. Use of such grafts cut from avulsed human scalp seems to present the only feasible way to achieve hair covering of the head after scalp avulsion.

Theoretical and technical considerations. Dermatome donor sites heal by metaplasia and spreading outgrowth of epithelium derived from sweat glands and hair follicles which have been cut across. Free, thin, deeply cut (split-split) grafts have been used to provide surface covering epithelium. In the human scalp (as in the pig skin), hair follicular structures extend to the surface, with cellular elements which produce hair shafts lying in the fat of the superficial fascia (Figs. 5 and 6). Even so, it is common to see growth of fine, brittle, unserviceable hair from thin superficial dermatome grafts taken from sites where hair had grown—as the thigh, or the head, in the case reported above. This indicates some power of regeneration of the superficial fragments of hair follicles transplanted in a skin graft. The elements left in situ (at donor sites) characteristically bear normal hair. Secondly, it is recalled that free

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thin graft skin from avulsed masses of tissue for immediate wound covering, and grafting varicose ulcers (when an ellipse of skin was excised from a previously made high saphenous ligation incision). In other circumstances where loose skin can be excised with primary side-to-side closure of wound edges, the problem of variable healing of the usual dermatome donor site (especially when thick grafts are employed) is completely avoided. The free graft present on the dermatome drum can then be resplit to increase the amount of serviceable ordinary graft skin available, or, as in the experiments described, to secure calibrated, even thickness grafts taken from a level below the epidermis. In re-splitting, the blade is carried on around the back of the dermatome so as to arrive again at its starting position, and the scale is reset so as to cut away and leave behind whatever thicknesses are desired. It is usually helpful, unless very thick grafts are being made, to place the blade just over the leading edge of the skin on the drum (it should be set at about .015 inch thicker for this maneuver), and then, in the new position, be set back to the final reading. This will compress the skin at the leading edge beneath the blade, but facilitates starting the second cutting. If there has been rolling of the skin edges locally, thinly applied additional cement may help to reapply them, and the assistant's finger tips will insure the result as described (see Fig. 4). It is not practical to remove the graft remaining on the drum for reapplication of cement. Use of nylon or pliofilm[14] backing interferes with close application of grafts to curved surfaces such as those presented by the cranial vault. When used to increase the yield of limited donor sites, serviceable split-split grafts as thin as .006 to .008 inch may be made (thus giving a threefold increase to an initial graft cut at .024 inch; the deeper layers of these grafts heal more slowly than do those which include the epidermis, but usually produce serviceable skin which cannot be distinguished from that derived from the conventional dermatome graft. Healing must occur as in the usual dermatome donor site where there is no basal cell layer remaining (as is quite regularly the case if a graft thicker than .008 inch is taken) by metaplasia and outgrowth of epithelium from sweat glands and hair follicles. The rubber cement employed does not stick to the operator's gloves and to instruments, and grafts removed from the drum are easily handled, the drum being cleaned by simple wiping. It is easily appreciated that the Padgett dermatome, with the use of split-split grafts, presents many possibilities in the management of scalp avulsions, and that the problems which beset those who have considered using razor grafts, trimming with a scalpel, etc., may be overcome.

skin grafts must be as thin as possible, since with increasing thickness the amounts of viable grafted skin decrease and require more ideal recipient sites (as regards vascularity, absence of actual or potential bacterial infection, close application of grafts, immobilization pressure dressings, etc.). Therefore, it was decided to evaluate density and quality of hair growth (if any) in grafts of different thicknesses taken from different depths, employing the split-split technic described, using young pigs. Superficial layers cut away were therefore discarded in the interest of securing thinner grafts, and it was thought that the deeper sections of hair follicles (containing at least part of the actual germinal portions) would undergo more regeneration than do the superficial ones—epithelial covering being derived from the sources mentioned as in any

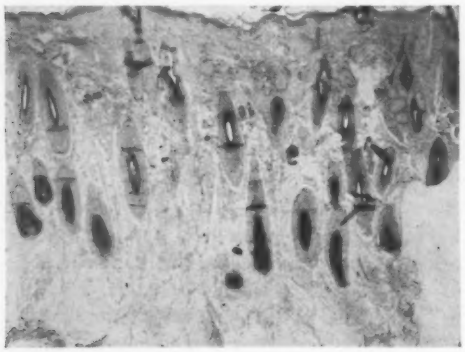

FIG. 5

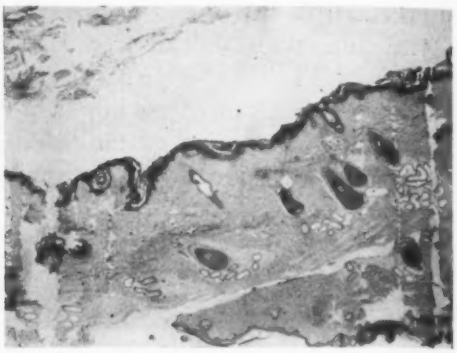

FIG. 6

FIG. 5.—Photomicrograph of normal human scalp shows thickness, number, and depth of hair follicle elements; compare with Figure 6 (x 22).

FIG. 6.—Photomicrograph of normal pig skin demonstrates similarity to human scalp, although it is not quite so thick, and hair follicles are fewer in number, with less dispersion in depth (x 22).

split-split graft or donor site. As described below, in Pig. No. 2, sections of graded thickness from varying depths were tested; in Pig No. 6, large sections gave predictable results and illustrations shown were made of these (Figs. 7, 8, 9, 10, 11 and 12). That thin grafts do regenerate and produce both serviceable hair and normal covering epithelium is illustrated (Figs. 13 and 14), a

FIG. 7.—Grafts made for illustration are shown here with one graft cut as indicated and sutured in place while second graft is being cut away.

FIG. 8.—End results of grafts are shown with indicated thickness and depth; note appearance of external surface of deep split grafts. Continuous wire sutures were used.

FIG. 9.—Growth of hair from graft BC is shown to be of reduced density as well as poor quality; compare with adjacent normal hair. The lower half of this graft failed to grow, as indicated by the scar.

FIG. 10.—Growth of hair from graft D is seen to be mostly of good quality but present in much reduced amount.

FIG. 11.—Growth of hair in BCD graft shows uniformly excellent quality but markedly variable density; this was due to variation in thickness of original graft.

FIG. 12.—Growth from DE is seen to present nearly normal hair with good quality and density.

FIG. 7

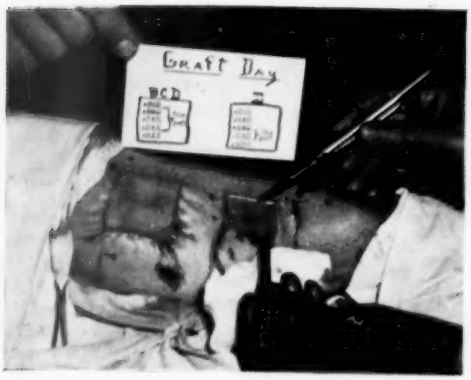

FIG. 8

FIG. 9

FIG. 10

FIG. 11

FIG. 12

section cut at .015 in. being seen to grow into nearly normal pig skin in every respect.

Delayed skin grafting over large amounts of granulation tissue gives rise to relatively avascular scarring and demonstrates thin, atrophic, easily eroded, ulcerating, unserviceable epithelium. If the failure of hair to grow over ordinary skin scars, even where there has been no loss of tissue, is recalled, one may appreciate the devastating effect of scar tissue on cosmetic and functional results with respect to hair growth, and may appreciate the desirability of *immediate* reconstruction of any denuded body surface. Another factor which seems to make epithelium growing over scar tissue less than perfectly serviceable is the absence of the normal cushioning effect which subcutaneous fat provides against ordinary traumata. No solution to this problem is apparent,

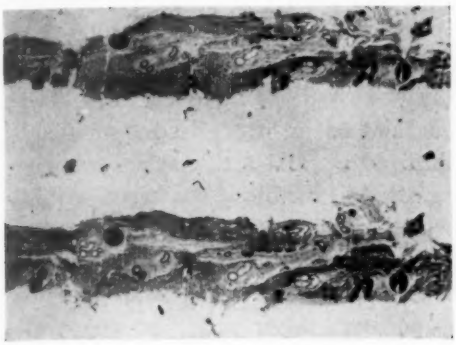

FIG. 13

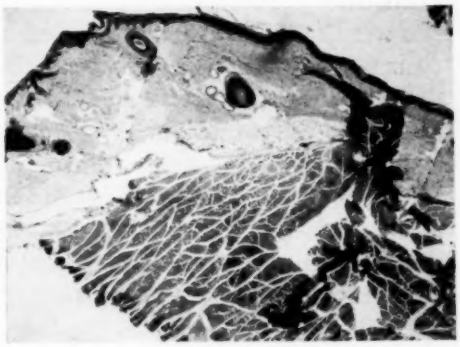

FIG. 14

FIG. 13.—Photomicrograph demonstrates elements actually present in a deep split graft of pig skin which comprises ½CD. The sections are cut somewhat obliquely, so that fair estimate of cellular elements can be made concerning this graft, only .015 in. in thickness (x 22).

FIG. 14.—Photomicrograph shows regeneration of graft ½CD illustrated in Figure 13 after 60 days. This graft bore hair nearly normal in quality and density (x 22).

but the author has attempted free fatty tissue grafting, with shortly delayed application of thin covering skin grafts with varying success in one difficult situation. When technical problems which arose can be overcome, the method may prove to have some value.

For this testing, young pigs (15 to 20 lbs., 3 to 4 weeks old, and recently weaned) were employed because of the similarity between their skin and human scalp with regard to overall thickness, and number and location of hair follicles (Figs. 5 and 6). Certain criticisms of the experiment are immediately apparent; results of animal experiments must be applied in treatment of human patients with caution. The pigs were young and the powers of all young animals to heal and regenerate function by altered tissues are well known. Also, the human pericranium may be a less perfect recipient site for grafts than the fatty tissue of the young pig's back. In addition, there will probably be found

differences between the young and the aged among human patients, between those whose hair varies in amount and character, between sexes, and perhaps even depending upon hair color, race, etc. These points await further elucidation, but it seems likely that the experiments described here fairly duplicate conditions which are seen with human scalp avulsion, particularly when the experience with the case reported is considered.

One anesthesia accident and one experimental failure should be mentioned, that some future investigator may profit from the experience past. It is difficult exactly to control the depth of ether (inhalation) anesthesia in the pig, and long plastic procedures require constant attention to this. Most of these experiments were performed with slow intravenous drip of dilute solutions of sodium pentothal, and the animals were fastened to the operating table with ties placed around the lower legs. At the conclusion of the first experiment, after the animal had been in excellent condition for seven hours, all four ties were released quickly. The feet were noted to be somewhat swollen and cyanotic, and within one minute there was complete respiratory stoppage. Cardiovascular function remained apparently normal for many minutes, thus differing from tourniquet shock. The animal did not recover, despite administration of respiratory stimulants and prolonged manual artificial respiration. It seemed that sodium pentothal had been pooled in the blood contained within the lower extremities beyond the ties—which acted as tourniquets—and the amount returned after their release was lethal. This explanation was further substantiated when, with Pig No. 2, the ties were released singly at ten minute intervals, with deepening of the level of anesthesia after each was removed. This animal was given supportive intravenous saline and glucose during operation, and other experimental animals were tied only during induction of the anesthesia. Pig No. 6 was treated under inhalation open ether anesthesia, which is easily used for short procedures and does not require time consuming cannulation of the veins under local anesthesia. Local anesthesia was tried for the grafts, but is not satisfactory with the pig; the light anesthesia which may be maintained with dilute intravenous barbiturates is ideal for these long procedures which require a minimum of sensory dulling and no relaxation. Vocal cordectomy (best performed in the pig through an anterior neck incision) is helpful but not essential. All wounds were dressed with petroleum jelly-impregnated gauze, surgical sponges, and circular Elastoplast bandages (which remained intact for about six days, when first dressings were done).

In one experiment an attempt was made to bury a large, thick piece of skin from the surface of which a .020 inch dermatome graft had been removed. It was planned to allow vascularization of this tissue from both sides while it was entirely enclosed under an envelope flap on the side of the animal opposite the donor site, which had been covered with the superficial graft cut away. Then, in delayed stages it was planned to free first one side and then the other, developing a pedicled flap which could be "waltzed" back to the defect ending up with the right side up in its original place, the dressing graft being

cut away just before replacement. This could not be completed because of a low-grade, anaerobic infection which supervened, and because of contracture and invasion of scar tissue growing in from the recipient site. Margins of the buried graft piece were difficult to identify in spite of fine wire guide sutures. This method resembles in some respects that employed by Harkins[5] and might entail some of the problems which he described in connection with the use of superficial and deep cutis grafts in reinforcing the repair of large ventral and incisional hernias. Butcher[1] found that sections of skin transplanted subcutaneously and intraperitoneally in the rat progressively lost their hair-forming elements, and formed epithelium lined sacs about their superficial surfaces.

Grafts and results. The notation used to describe thickness and depth of the grafts employs a system of letters in lieu of the more cumbersome description in terms of thousandths of inches (the Padgett dermatome is unfortunately calibrated in the English rather than the metric system, and conversion of figures to the latter would cause unnecessary confusion). The most superficial 10/1000 inch of the graft is designated by the letter "A," the letter "B" indicating only the tissue which lies between 10 and 20/1000 inches, "C" the next 10. Thus, a graft described as "BCD" is one taken by cutting across full thickness skin with the dermatome set at .040 inches, then recut at .010 inches, the intermediate section so derived being employed, the most superficial sheet of skin (that applied directly to the dermatome drum) being discarded. Similarly, graft "½CD" is derived by cutting with an initial setting of .040 inches, then recutting at .025 inches, discarding the .025 inch graft remaining on the dermatome drum. Grafts referred to below were made and handled according to the methods already described, Zenker-fixed biopsies being taken and studied in section for all grafts. The work was repeated with animals numbered 4 and 5 but, as results were quite comparable to those described, they are not recounted.

Pig No. 2: Seventeen grafts measuring 2 to 3 cm. on each side were taken serially along the two sides of the animal's thorax and abdomen, the grafts being varied according to thickness and depth, as indicated in Table I. There were only three nearly complete failures to grow; the general success in growth is indicated in the table, desquamation of an appreciable amount of superficial tissue, exudate, or both being noted. Final hair quality (here evaluated after 52 days) is indicated on a scale whereby + represents fine, easily fractured hair, ++++ indicates grossly normal hair which appears to be identical with that of the undisturbed adjacent skin. Density of growth of the hair was seen to vary, and this is again graded on a scale of + to ++++ where + indicates presence of only occasional hairs and ++++ shows that the regrown hair is of the same density as that of the normal skin. O signifies absence of any hair, and ± means that there were present only rare, isolated hairs.

Pig No. 6: Table II indicates the results secured with the last animal, whose grafts are pictured during their performance (Figs. 7 and 8), and in

their final stage after 63 days (Figs. 9, 10, 11, and 12). These grafts were made for purpose of illustration with the method which was quite predictable.

Certain conclusions seem to be warranted from a study of these tables:

1. Layer "D" is usually essential for growth of hair of good quality; thus, a certain minimum depth of graft must be used to avoid growth of slender, brittle, unserviceable hairs.

TABLE I.—*Pig No. 2. Tabulation of grafts employed, character of growth, and description of hair after 52 days.*

Graft No.	Layers Employed	Success of Initial Growth	Final Hair Quality	Final Hair Density
1	A	Good	0	0
2	AB	Good	0	0
3	ABC	Good (Superficial desquamation)	+	+
4	ABCD	Excellent	++	++
5	ABCDE	Excellent	++++	+++
6	B	Good	0	0
7	BC	Good	0	0
8	BCD	Nearly complete loss	0	0
9	BCDE	Good (Superficial desquamation)	++++	++
10	C	Good	0	0
11	CD	Good, plus	++++	++
12	CDE	Good, plus	++++	++
13	D	Good	++++	+++
14	DE	Good	++++	+++
15	E	Fair, plus	++++	+
16	DE with the underlying .040 inches	Complete loss	++++	—
17	Full thickness	Fair (Apparent superficial slough)	++++	—

TABLE II.—*Pig No. 6. Tabulation of grafts employed, character of growth and description of hair after 63 days (see Figures 7, 8, 9, 10, 11, and 12).*

Graft No.	Layers Employed	Final Hair Quality	Final Hair Density	Comment
1	BCD	++++	+ to ++++	Probably variable thickness graft
2	D	++++	+ to ++	Probably variable thickness graft
3	BC	++	+	
4	DE	++++	++++	Near normal hide

2. The final *effective* thickness of the grafts largely determines the density of hair growth. It must be remembered that the many factors described may alter the thickness at which the dermatome is actually cutting; beyond this, any important loss of tissue, however diffuse, and however adequate the final epithelial covering may be, during the healing phase will decrease what is termed final effective thickness.

3. There is extensive regeneration of hair forming elements, even taken in small fragments (see Figs. 13 and 14), so that, in the young pig, entirely normal hair bearing may be anticipated from grafts as thin as .015 inches taken from the proper depth.

Case 2.—(Boston City Hospital No. 1313009.) P. C., a 72-year-old white male, was admitted to the Fifth Surgical Service, Boston City Hospital, on February 16, 1949, because of an ulcerated, foul-smelling tumor mass which had grown on his right occipital scalp during the preceding 14 months.

Past history was of interest in that patient had had increasing exertional dyspnea, orthopnea, ankle swelling and productive cough for many years. There was no suggestion of previous angina or myocardial infarction.

Physical examination demonstrated an aged, ill-appearing white male with evidences of cardiac decompensation. Blood pressure was 160/40, pulse 80, normal sinus rhythm. Peripheral arteries were tortuous and beaded. There was well marked venous distention seen about the face, neck and all 4 extremities (pressure measured at 45 cm. of water in both arms and legs). There was 3 to 4 plus soft, pitting edema over the sacral region and both lower legs. The liver was enlarged 5 cm. below the right costal margin and was slightly tender. The heart was enlarged to the left on physical examination and by chest roentgenogram. Electrocardiogram was interpreted as within normal limits. On the right occipital scalp there was present a foul-smelling, ulcerated, black, raised tumor mass with well defined borders measuring 14 by 9 cm. In the scalp about the tumor there were some streaks of purple discoloration. These suggested infiltrative growth.

Laboratory Examinations: Urine, white blood count, Hinton, N.P.N., prothrombin time, icteric index, P.S.P., cephalin flocculation and alkaline phosphatase were all within normal limits. Total protein was 5.3 Gm. 100 cc.; hematocrit 28; hemoglobin 9.5 Gm. 100 cc. Metastatic and stereoscopic skull roentgenograms were normal. Culture from scalp region showed *B. pyocyaneus,* alpha hemolytic streptococcus, hemolytic staphylococcus aureus, and *B. coli.*

It was felt that the patient presented arteriosclerotic heart disease with marked decompensation, although possibility of metastatic mediastinal tumor with great vein obstruction could not be excluded and fluoroscopic examinations were equivocal. The low serum protein level was felt to be only contributory to the peripheral edema. Accordingly, the patient was treated with digitalis, mercurial diuretics, ammonium chloride, salt restriction and high protein diet. The scalp tumor was biopsied, and although interpretation of the section was difficult because of marked inflammatory reaction, it was initially reported as hemangioma. By the fifteenth hospital day the patient's general condition was markedly improved and venous distention had cleared. On this day, using one per cent procaine field block anesthesia, the full thickness of scalp bearing the tumor was excised to include a 2 cm. border of normal scalp about it. Periosteum under the scalp demonstrated definite fibrosis and thickening and one area 4 cm. in diameter was seen to be discolored, purplish-red, and had clinical appearance of infiltrative growth of tumor. This periosteum was accordingly excised and stripped cleanly away from the outer table. In preparation for grafting this area a portion of outer table was cut away with a sharp osteotome but the area was not entirely unroofed because it was feared that duration of operation and trauma to the patient would be excessive. The corresponding piece of normal scalp from the opposite side, about 12 cm. in diameter, was then excised, leaving intact periosteum, and after hemostasis had been secured around the entire field, the scalp was divided into two sections and placed on the dermatome according to the technic described before for splitting into layers. Dermatome cutting was then done at .055 and again at .02 in. Preparation of the split grafts was very successful and the four pieces thus produced were then sutured in place to cover the entire defect over the cranial vault using continuous fine steel wire sutures. Petroleum jelly gauze, dry sterile sponges and elastoplast

bandage were employed for dressing, and during the last part of operation the patient was given 500 cc. of cross-matched, citrated whole blood, very slowly. The patient did well postoperatively for 4 days. Because of the relatively severe degree of anemia he was slowly given transfusions on the second and third days. On the fifth postoperative day the wound was dressed and the grafts were seen to be almost entirely viable except for the area lying over the denuded outer table where periosteum had been removed. The deep split grafts had the appearance of granulating surfaces and were exuding blood at this time. Wet saline dressings were instituted. During the second week after operation cardiac decompensation again became evident, with increasing severity. Fluoroscopic study was twice performed to ascertain possible presence of pericardial effusion, and on the eleventh and twelfth postoperative days 1350 and 700 cc. of clear yellow fluid were aspirated from the right pleural cavity. Despite continued treatment, his venous distention returned to levels higher than that noted on admission and he expired on the twelfth postoperative day. On the day of exitus the deep split grafts had progressed to epithelialization which was almost complete, the total amount of take being estimated at 95 per cent, and a stubble of hair was visible and palpable on the deep split grafts.

Histological examination of the excised tumor had demonstrated that it was in fact a hemangiosarcoma with histologic appearance of high degree of malignancy. Complete autopsy examination showed no evidence of tumor metastases, but an advanced state of arteriosclerosis with arteriosclerotic heart disease, pulmonary congestion, edema, ascites, peripheral edema, hepatic congestion and other evidences of severe cardiac decompensation.

Thus, clinical application of the method derived from pig experimentation is herein reported. Unfortunately, this patient lived only 12 days after scalp reconstruction using both superficial and deep split layers to cover a very extensive denudation of the pericranium. However, during the period of observation it was determined that the deep split layer of the scalp would grow and did produce covering epithelium. Growth of hair from this layer was seen to have started after 12 days. This is interesting in that in the young pigs reported above hair growth began at a slow rate and was never evident within the first three weeks.

CONCLUSIONS

From the considerations, experience, and experiments recounted, it seems that greatly improved results may be secured in treating those patients who suffer extensive scalp avulsions, those who lose large amounts of hair-bearing scalp through burning, because of infections, or after extensive resections for malignant neoplasm. The method suggested is probably not as reliable as reconstruction with pedicled flaps when that is possible, and should not, of course, be employed when avulsed scalp is still attached by any reasonable pedicle. It would not seem warranted for use in cosmetic repair of the alopecia of age, alopecia areata, etc. The author recommends cutting grafts including "½CDE" or "DE", between 25 or 30/1000 and 50/1000 inches, remembering that the ideal graft for these reconstructions is one thin enough to have reasonable expectation of viability, thick enough to be easily cut and handled and to bear a sufficient density of hair, and deep enough to assure the growth of hair that will be serviceable and of good quality. Denudation of the outer table of the skull of its periosteum must be recognized and treated as indicated, and the countless other details concerned with caring for the patient and the wound must all be attended for good results. Lastly, the surgeon must remember that the best reconstruction time after scalp avulsion is a short-lived one, and does not return.

SUMMARY

1. The problem of scalp avulsion is outlined.

2. A case is reported wherein immediate grafts were taken from the avulsed scalp itself.

3. Principles and problems concerned with grafting after scalp avulsion with and without loss of periosteum, and technic of "split-split" grafting with the Padgett dermatome, are discussed.

4. The theoretical basis and practical achievement of thin grafts which bear normal hair on the pig are recorded.

5. Clinical application of the experimental method with the human scalp is reported, with evidence that epithelial covering and hair growth progress rapidly.

6. A treatment for scalp avulsion designed to secure normal hair over the head is recommended.

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ARTERIAL ANEURYSMS*

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THERE HAS NEVER been published a better review of the subject of aneurysm than the one by Matas[6] in Keen's Surgery in 1916. The 72 aneurysms operated upon and 40 aneurysms "wired" at the Johns Hopkins Hospital were reported by Reid[7] in 1926. In 1933 Elkin and Campbell[4b] reported the 44 cases of arterial aneurysms upon which they had operated. There have been recent reports of large numbers of cases of traumatic aneurysm which occurred during World War II.[4a, 8] Although the number of patients to be presented in this article is not large, it is thought justifiable to record our observations, including follow-up data, on the aneurysms which have been operated upon in a university hospital over a period of 24 years (1925–1948).

INCIDENCE

General. In the Vanderbilt University Hospital since 1925, 26 arterial aneurysms have been subjected to operation. Five of these patients have been previously reported (Cases No. 1, 2, 3 and 4, by Brooks[1] and No. 22 by Daniel[3]). In addition to the 26 patients herein discussed, there have been two patients operated upon with aneurysms of the thoracic aorta, one of whom died as the chest was being opened and another who was subjected only to exploratory thoracotomy. In 1938, Kampmeier[5] reported 75 aneurysms of the thoracic aorta from this clinic. Since that time 59 aneurysms of the thoracic aorta have been observed in this hospital. An aneurysm of the abdominal aorta has been seen in each of two patients, neither of whom was subjected to operation, the diagnosis in both of these having been made upon postmortem examination. During the years from 1925 through 1948, 11 operations have been done upon intracranial aneurysms and 33 upon peripheral arteriovenous fistulas. The arteriovenous fistulas will be the subject of a subsequent report.

Race, Sex, Age, Type. There were 17 white patients and nine Negroes, although the ratio of white patients to Negroes admitted to the Vanderbilt University Hospital is 9 to 1. There was only one female patient (Case 5). The youngest patient was six months and the eldest was 64 years of age (Tables I and II). There were 16 true and 10 false aneurysms.

Site. The sites at which the aneurysms occurred are shown in Table III and Figure 1. Thirteen, or half of them, were in the lower extremity, 12 of these having been in either the femoral or the popliteal artery. Eight aneurysms occurred in the upper extremity, four in the trunk, one in the region of the head and face, and none in the neck.

* Submitted for publication September, 1949.

CAUSES

Traumatic. Even in civil practice, trauma was the most frequent single cause of aneurysm, ten of them having been due to injury (Table IV). Seven of the lesions were caused by bullets, one by a knife, one by a surgical needle and one by an intravenous needle.

Syphilitic. The Wassermann or Kahn reaction was positive in seven of the patients in whom there was no direct wound. However, there was no absolute

TABLE I.—*Age in Decades.*

Years	No. of Patients
0–9	1
10–19	3
20–29	4
30–39	6
40–49	2
50–59	5
60–64	5

evidence in any of them that syphilis caused the aneurysm, that is, the treponema pallidum was not demonstrated in the microscopic sections of the sac of the aneurysm, in the instances in which the sac was excised, nor did the sections show the characteristic microscopic pathologic changes of syphilis. Cases 2 and 16 showed microscopic evidence of arteriosclerosis. Furthermore, physical examination of four (Cases 10, 11, 13 and 16) of these seven patients

TABLE II.—*Ages of Patients with Aneurysms Other Than Traumatic or Mycotic.*

Decades	No. of Patients
0– 9	0
10–19	0
20–29	1
30–39	3
40–49	1
50–59	5
60–69	5
Average age	51
Below 50	5
Above 50	10

showed arteriosclerosis and one of the four (Case 10), who had an aneurysm of the superior gluteal artery, had received injections of bismuth into the buttocks. Thus in only two of these seven aneurysms, one of the dorsalis pedis artery (Case 6) and one of the radial artery (Case 17), there was no known etiologic factor other than syphilis. There were possible precipitating factors in three patients in that one had done unusually heavy work shortly before the appearance of the aneurysm (Case 11), another had lifted a heavy weight (Case 13), and a third had received a slight blow upon the area subsequently found to show an aneurysm (Case 16). All seven patients were colored males, two were aged 36 and 38 and the ages of the others ranged from 55 to 68.

An attempt was made to determine the length of time which had elapsed between the initial infection with syphilis and the occurrence of the aneurysm. Four patients denied having had a primary lesion. One patient (Case 10) described lesions which might have been the secondary skin rash of syphilis, which occurred ten years before the occurrence of the aneurysm. One individual (Case 17) had had a penile sore 20 years before and a third (Case 13) had had a penile lesion 30 years previously.

Arteriosclerotic. Two of the aneurysms (Cases 9 and 25) were thought to have been due to arteriosclerosis. In both of these patients there was definite generalized arteriosclerosis and in neither was there clinical or serologic evidence of syphilis.

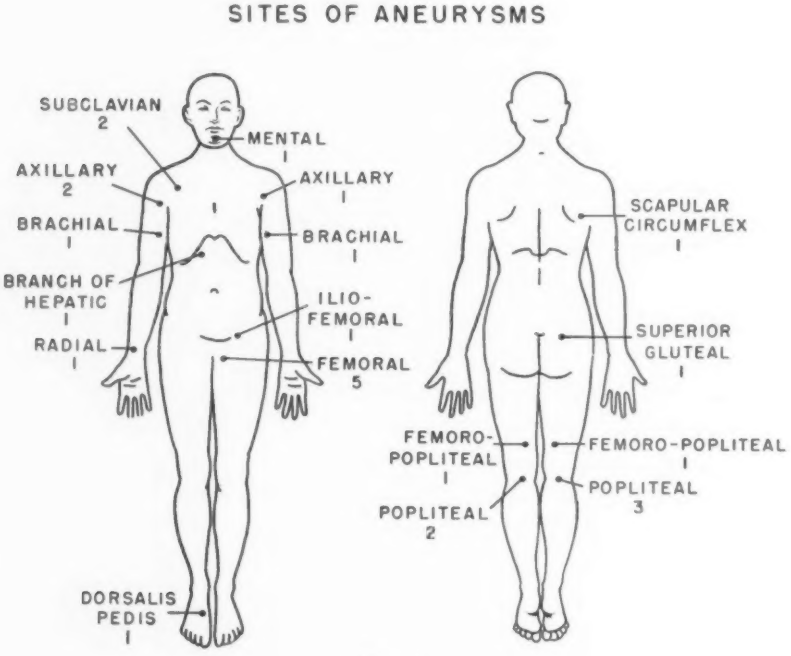

FIG. 1

Mycotic. An aneurysm of the subclavian artery in a child (Case 22) was thought to be secondary to inflammatory disease in a lymph node which was in contact with the artery. This patient was reported by Daniel[3] in 1945.

Spontaneous. Aneurysms occurred in six patients in whom there was no injury, no clinical or laboratory evidence of syphilis and no demonstrable arteriosclerosis. However, as the ages of three of these patients were 58, 60 and 61 (Cases 14, 12 and 8) arteriosclerosis might possibly have caused the original disease of the arteries. One patient (Case 21) had dilated arteries of the trunk secondary to coarctation of the aorta and the aneurysm of the scapular circumflex artery was unquestionably related to the aortic lesion. In two other patients, an aneurysm of the axillary artery in a man of 45 (Case

4) and of the mental artery in a woman of 25 (Case 5), the aneurysms must be called truly spontaneous.

TYPE

All ten of the traumatic aneurysms were false and the 16 aneurysms which were thought to be syphilitic, arteriosclerotic, mycotic or spontaneous were true aneurysms.

TABLE III.—*Sites.*

Lower Extremity	
Femoral	5
Femoro-popliteal	2
Popliteal	5
Dorsalis pedis	1
Total	13
Upper Extremity	
Subclavian	2
Axillary	3
Brachial	2
Radial	1
Total	8
Trunk	
Scapular circumflex	1
Superior gluteal	1
Branch of hepatic	1
Iliofemoral	1
Total	4
Head*	
Mental	1

* There were also 11 patients with intracranial aneurysms who were subjected to operation.

TABLE IV.—*Causes.*

Traumatic		10
Bullet	7	
Knife	1	
Suture needle	1	
Intravenous needle	1	
Syphilitic (?)		7*
Spontaneous		6†
Arteriosclerotic		2
Mycotic		1
Total		26

* Five of these seven patients had arteriosclerosis.
† One of these six patients had coarctation of the aorta.

SYMPTOMS

Pain. Pain had been noted by the patients in all instances except three. In the individuals who had no pain, the aneurysms were present in the

mental, radial and subclavian arteries. The latter patient was a six-month-old child.

Mass. A mass had been noted by all patients except one (Case 22). The duration of the mass before admission to the hospital ranged from three days (Case 21) to 32 years (Case 14).

Rupture. Rupture of the aneurysm occurred before admission in only one instance (Case 26). However, rupture was thought to be imminent in one (Case 3) and in another (Case 19) it occurred on the operating table while the skin was being prepared for operation.

Gangrene. Preoperative gangrene occurred in only one instance (Case 9).

PHYSICAL FINDINGS

The four characteristic signs of aneurysm (mass, expansile pulsation, thrill and bruit) occurred as follows:

Mass. There was a palpable mass in each of 25 patients and in the twenty-sixth patient (Case 22) a mass was visible on the roentgenogram.

Pulsation. Pulsation was noted in 22 patients, in 20 of whom it was expansile. The instances in which pulsation was absent were in aneurysms of the brachial, axillary, subclavian and a branch of the hepatic artery (Cases 15, 1, 22 and 25).

TABLE V.—*Patients with More Than One Aneurysm.*

Case No.	Cause	Location of Primary Aneurysm	Location of Other Aneurysm
9	Arteriosclerotic	Popliteal, left	Popliteal, right
16	Syphilitic	Iliofemoral	Innominate
21	Spontaneous*	Scapular circumflex	Middle cerebral
25	Arteriosclerotic	Branch of hepatic	Thoracic aorta

* This patient had coarctation of the aorta.

Thrill. The presence of a thrill was recorded in only eight instances but it is possible that it might have been present in other patients and not recorded.

Bruit. A bruit was heard in 19 patients. In the 16 (of the 19) patients in whom the timing was recorded, it was noted to be systolic. Descriptive adjectives applied to the characteristics of the bruit were blowing, shrill, rough and harsh.

In the only patient (Case 22) in whom all four signs were absent, an area of increased density was seen on the roentgenogram. There were three patients (Cases 1, 22 and 25) in whom there was no pulsation, thrill or bruit. All four signs were present in seven patients.

Patients with more than one aneurysm (Table V). In one patient (Case 25) there was "uncoiling" of the aorta which could have been called an aneurysm. In one individual (Case 9) there was an aneurysm of the opposite popliteal artery. One patient (Case 16) had an aneurysm of the innominate artery and a fourth patient (Case 21) died following rupture of an aneurysm of the middle cerebral artery.

Cyanosis. Cyanosis of a part of the extremity was noted before operation by the staff in three instances (Cases 2, 4 and 20), in addition to the patient (Case 9) mentioned above, in whom gangrene was present.

DIAGNOSIS

A preoperative diagnosis of aneurysm was made in all instances except two, the aneurysm of the subclavian artery in the infant and of the branch of the hepatic artery. In each of these patients the aneurysmal sac was almost completely filled with laminated clot.

TABLE VI.—*Data on Patients in Whom Amputation Was Necessary.*

Case No.	Age	Type	Cause	Preoperative Gangrene	Operation	Ligation of Vein	Exercises	Interval Between Primary Operation and Amputation (Days)
8	61	True	Spontaneous	Absent	Aneurysmectomy	Yes	Yes	18
9	59	True	Arteriosclerotic	Present	Aneurysmectomy	Yes	No	3
11	50	True	Syphilitic	Absent	Proximal ligation	No	No	76

OPERATIVE PROCEDURES

The operative procedures are listed in Tables VI to XII. In aneurysms of arteries which can be ligated without jeopardizing the life of the tissues they supply, complete aneurysmectomy is the procedure of choice. However, in aneurysms of essential arteries we believe that function of the extremity is better if the artery is saved. Therefore, in such arteries we recommend

TABLE VII.—*Results of Complete Aneurysmectomy.*

Case No.	Artery	Results
3	Femoro-popliteal	Good
5	Mental*	Good
6	Dorsalis pedis*	Good
8	Popliteal	Amputation
9	Popliteal	Amputation†
17	Radial*	Good
18	Femoral	Fair
21	Scapular circumflex*	Good
25	Branch of hepatic*	Good

* Blood supply adequate even if involved artery is excised.
† Had gangrene of toes before operation for aneurysm.

reconstructive or restorative aneurysmorrhaphy or, if such procedures are impossible, obliteration of the aneurysm by sutures placed within the sac. We believe that as much of the sac as possible should be excised without injuring collateral circulation or adjacent nerves. Following complete aneurysmectomy, if the continuity of the artery can be re-established by anastomosis with or without some type of graft, such a procedure should give excellent results. Sympathetic ganglionectomy was not done in any of our patients. The concomitant vein was ligated in four patients (Cases No. 2, 8, 9 and 14) and at operation was noted to be thrombosed in two instances (Cases No. 3 and 26).

POSTOPERATIVE TREATMENT

In the postoperative care of extremities in which the blood supply is inadequate, three important points will be discussed.

Despite the fact that the work of Brooks and Duncan[2] showed conclusively that tissues of questionable viability are more likely to survive at low than at high temperatures, many physicians still use the hot water bottle and the electric light cradle on such tissues. In some patients herein reported, the electric light cradle was used but that mistake has not been made in this clinic in the past 13 years. The involved extremity should never under any circumstances be heated above room temperature.

The second point is in relation to the position of the extremity. In view of the fact that every normal adult is familiar with the law of gravity, it is amazing that, in the management of arterial disease, physicians continue to

TABLE VIII.—*Operative Procedures and Results.*

Operation	No. of Patients	Results		
		Amputation	Good	Fair*
Aneurysmectomy, complete	9	2	6	1
Partial aneurysmectomy with obliterative aneurysmorrhaphy	6	0	5	1
Obliterative aneurysmorrhaphy	4	0	3	1
Proximal ligation	2	1	1	0
Proximal and distal ligation	2	0	1	1
Restorative aneurysmorrhaphy	1	0	1	0
Restorative aneurysmorrhaphy and partial aneurysmectomy	1	0	0	1
No treatment	1	0 (Died)	0	0

* The results in five patients were considered to be fair because they had slight limitation of function.

elevate extremities. The position in which the tip of the extremity receives the most blood is that in which it is furthest below the level of the heart. Thus, the most blood reaches the foot when the patient stands erect. However, because the venous return is diminished in this position, it is not the position of election. We believe that the correct position is obtained by lowering the extremity so that it is about halfway between the horizontal and the vertical. This position is achieved by elevating the head of the bed (not just the trunk of the patient) in arterial disease of the lower extremity, and elevating the trunk, with the arm at the side, in arterial disease of the upper extremity.

The third point concerns the movement of the extremity. The beneficial effect of Buerger's exercises upon thromboangiitis obliterans is well known, but the beneficial effect of similar pumping motions in the postoperative care of extremities in which the blood supply is inadequate has never been emphasized. The extremity should be elevated for about one minute, then hung off of the bed for approximately three minutes, then returned to the position of election for three to five minutes. The angle to which the extremity should be elevated and the exact number of minutes during which it should remain in

each of the three positions are determined by the observation of its blanching and flushing. It is well known that the blood supply of an extremity is the poorest immediately after ligation of its main artery and that the blood supply improves every minute thereafter. Therefore, one should use every means possible to preserve the nutrition of the tissues during the immediate postoperative period because if they survive that period the collateral circulation may subsequently be adequate. Hence the exercises described should be kept up continuously for 24 or 48 hours, or until one is perfectly certain that the blood supply is adequate or until it is obvious that gangrene has occurred.

TABLE IX.—*(Results Cont'd) Patients with Slight Limitation of Function.*

Case No.	Artery	Operative Procedure
4	Axillary	Obliterative aneurysmorrhaphy Partial aneurysmectomy
18	Femoral	Aneurysmectomy
20	Axillary	Obliterative aneurysmorrhaphy
23	Femoral	Proximal and distal ligation
24	Popliteal	Restorative aneurysmorrhaphy Partial aneurysmectomy

These exercises have been used in this clinic for at least 14 years, and it is likely that at least three extremities would have required amputation if this maneuver had not been used (Cases 20, 23 and 26). It is possible that its use might have prevented the necessity for amputation in a patient who was operated upon over 14 years ago (Case 11).

The extremity should never be immobilized for two reasons. One is that the exercises described promote the formation of collateral circulation and aid

TABLE X.—*Results (Cont'd) Amputations (Three Patitnts).*

Case No.	Vessel	Procedure	Interval (Yrs.)	Present Status
8	Popliteal	Aneurysmectomy	14	Alive*
9	Popliteal	Aneurysmectomy	14	Alive and well
11	Iliofemoral	Proximal ligation	14	No recurrence

* Followed through letter.

in pumping blood to the limb. The second reason is that, because blood cannot flow into an area in which pressure on the soft parts is higher than that in the artery supplying the blood, the tissues which are in contact with the bed and bearing the weight of the extremity will receive insufficient blood.

In only one patient (Case 26) was paravertebral block done.

RESULTS

One patient (Case 22) died on the operating table. Follow-up data were obtained on the remaining 25 patients and are shown in Tables VII through XII. In no instance was there recurrence of the aneurysm.

Following operation upon the aneurysm, amputation was necessary in three instances (Table VI). The conditions common to the three patients

were that they were all over 50 years of age, the aneurysms were all in the lower extremity, and they were all true aneurysms. In Case 9 gangrene of the toes was present before operation and the circulation actually improved following aneurysmectomy. Examination of this patient 14 years after operation showed that the small aneurysm of the opposite popliteal artery had become obliterated spontaneously. In Case 8 it would have been better to obliterate the aneurysm and preserve the collateral circulation than to excise the aneurysm. In Case 11 the Hunterian operation was done, but not by choice. It was planned to control the blood supply by temporarily occluding the common iliac artery and then to proceed with operating upon the aneurysm of the iliofemoral artery. However, the patient developed circulatory

TABLE XI.—*Summary. A. Patients Still Alive.*

Case No.	History No.	Age	Cause	Vessel	Operative Procedure	Result	No. Yrs. Followed
2*	12760	36	Syphilitic	Popliteal	Obliterative aneurysmorrhaphy	Good	20
3*	23224	28	Traumatic	Femoro-popliteal	Aneurysmectomy	Good	19
4*	29276	45	Spontaneous	Axillary	Obliterative aneurysmorrhaphy, partial aneurysmectomy	Fair	18
5	37000	25	Spontaneous	Mental	Aneurysmectomy	Good	17
8	65776	61	Spontaneous	Popliteal	Aneurysmectomy	Amputation	14
9	66409	59	Arteriosclerotic	Popliteal	Aneurysmectomy	Amputation	14
11	67856	50	Syphilitic	Ilio-femoral	Proximal ligation	Amputation	14
14	74658	58	Spontaneous	Femoral	Obliterative aneurysmorrhaphy, partial aneurysmectomy	Good	13
15	76215	13	Traumatic	Brachial	Restorative aneurysmorrhaphy	Good	12
16	92083	64	Syphilitic	Popliteal	Obliterative aneurysmorrhaphy, partial aneurysmectomy	Good	10
17	94648	38	Syphilitic	Radial	Aneurysmectomy	Good	10
18	100544	39	Traumatic	Femoral	Aneurysmectomy	Fair	9
20	111672	32	Traumatic	Axillary	Obliterative aneurysmorrhaphy	Fair	7
23	137208	19	Traumatic	Femoral	Proximal and distal ligation	Fair	5
24	141247	26	Traumatic	Popliteal	Restorative aneurysmorrhaphy, partial aneurysmectomy	Fair	3
26	166396	45	Traumatic	Femoral	Obliterative aneurysmorrhaphy	Good	1

The result was considered good if there was no limitation of function and fair if there was slight limitation of function. There was no patient with marked limitation of function.

All patients were males except Case 5.

All patients were white except Cases 2, 10, 11, 16 and 17, who were Negroes.

* Previously reported by Brooks.[1]

failure and as it became necessary rapidly to bring the operation to a conclusion, this was done by ligating the common iliac artery and closing the wound. The procedure resulted in the cure of the aneurysm but in the necessity for subsequent mid-thigh amputation. In retrospect it is believed that it might have been better to close the wound and defer operation upon the aneurysm. Fourteen years after operation, examination of this man showed no evidence of recurrence of the aneurysm. In five of the nine patients subjected to complete aneurysmectomy (Table VII) the aneurysm was situated in a position where the blood supply is nearly always adequate, even if the vessel is extirpated. Of the remaining four patients, subsequent amputation

was necessary in two, evidence of circulatory deficiency (claudication) was present in one, and there was no evidence of circulatory deficiency in the fourth.

Nine patients died several months or years after operation (Table XII). The cause of death in the three patients in whom the aneurysm was due to trauma is irrelevant to this study. It is noteworthy that in five of the remaining six patients, death was due to disease of the blood vessels. Of the three patients who had had syphilitic aneurysms, two died of cerebral hemorrhage and one died of coronary occlusion. The patient who had had an aneurysm termed spontaneous, but which was secondary to coarctation of the aorta,

TABLE XII.—*Summary (Cont'd) B. Patients Who Died.*

Case No.	History No.	Age	Cause	Vessel	Operative Procedure	Interval Between Operation and Death	Cause of Death
1[a]	11928	17	Traumatic	Axillary	Proximal ligation	7 yrs.	Dementia paralytica
6	43285	55	Syphilitic	Dorsalis pedis	Aneurysmectomy	7 mos.	Cerebral hemorrhage
7	59037	27	Traumatic	Femoro-popliteal	Obliterative aneurysmorrhaphy, partial aneurysmectomy	12 yrs.	Coronary occlusion
10*	20101	63	Syphilitic	Superior gluteal	Obliterative aneurysmorrhaphy, partial aneurysmectomy	10 yrs.	Coronary occlusion
12[w]	44852	60	Spontaneous	Femoral	Obliterative aneurysmorrhaphy	2 yrs.	Pulmonary tuberculosis
13	71785	61	Syphilitic	Subclavian	Obliterative aneurysmorrhaphy, partial aneurysmectomy	8 yrs.	Cerebral hemorrhage
19[x]	107942	30	Traumatic	Brachial	Proximal and distal ligation	8 yrs.	Paresis
21[z]	125826	32	Spontaneous	Scapular circumflex	Aneurysmectomy	5 mos.	Ruptured aneurysm of middle cerebral artery
22[b]	134382	6 mos.	Mycotic	Subclavian	Exploratory thoracotomy	Died on operating table	
25[z]	130092	56	Arterio-sclerotic	Branch of hepatic	Aneurysmectomy	1 yr.	Coronary occlusion

[a] Previously reported by Brooks.[1]
[b] Previously reported by Daniel.[4]
* No recurrence 10 years after operation.
[w] No recurrence 2 years after operation.
[x] No recurrence 8 years after operation.
[y] No recurrence 5 months after operation.
[z] No recurrence 1 year after operation.
All above patients were white except cases Nos. 1, 6, 13 and 19. All were males.

died following rupture of an aneurysm of the middle cerebral artery. The patient whose aneurysm had been due to arteriosclerosis died of coronary occlusion.

In addition to the three patients subjected to amputation, 13 patients were alive at the time of this study. There was no evidence of recurrence of the aneurysm in any of them. In one of the 13 patients the aneurysm had involved the mental artery, in another it had involved the radial artery and in the remaining 11 patients large arteries of the extremity had been involved.

Each of the 11 patients was able to use the previously involved extremity to some extent, and in six of the eleven patients (Table XI) there was no limitation of function. In Case 18, an aneurysm of the femoral artery, and Case 20, an aneurysm of the axillary artery, the slight disability was due partially to nerve injury by the bullet.

SUMMARY

1. The clinical manifestations of 26 cases of aneurysms, their operative treatment, and the results thereof have been reported.

2. The postoperative management of extremities in which the viability of the tissues is questionable has been discussed.

CONCLUSIONS

1. Complete aneurysmectomy is the operation of choice for aneurysms of non-essential arteries.

2. In the treatment of aneurysms of essential arteries, complete aneurysmectomy, proximal ligation or proximal and distal ligation should never be done if it is possible to cure the aneurysm by any other operative procedure. However, following complete aneurysmectomy, if the continuity of the artery can be re-established by anastomosis, with or without some type of graft, such a procedure should give excellent results.

3. Following operation upon arteries, if the question of adequacy of circulation is present:

a. The limb should never be elevated for a long period of time.

b. Hot water bottles should never be applied to the limb.

c. An electric light cradle should never be used over the extremity.

d. The extremity should never be immobilized.

e. The exercises herein described should be used.

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STERILIZATION OF THE INTESTINAL TRACT BY ANTIBIOTICS AND SUPPLEMENTAL AGENTS*

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A CONSIDERABLE CHANGE has come to pass in surgery of the colon during the last decade. Although primary resection and primary anastomosis theoretically have always been procedures of choice, a prohibitive mortality previously limited their usefulness. That situation has now been almost completely reversed, and the mortality of the one-stage operation has been so greatly reduced that the patient's best interests are served by its performance whenever it is not contraindicated.

Chemotherapy and antibiotic therapy have played an important, though by no means the only, part in this happy development. The correction of dehydration, the maintenance of a proper fluid balance, the correction of anemia by massive blood transfusions, the correction of hypoproteinemia, and numerous advances in anesthesia must all share in the credit.

The first step in the accomplishment of effective antisepsis in gastrointestinal surgery was the preoperative use of relatively nonabsorbable sulfonamides, beginning with sulfanilylguanidine in 1940.[1] At the present time succinylsulfathiazole and phthalylsulfathiazole are most often used for this purpose.[2] They are highly effective. When they are employed in optimal dosages, the bulk of the stool is greatly reduced and the characteristic fecal odor is often eliminated because of the enormous reduction of the coliform bacterial content of the feces. To be more exact, by this method within five to seven days the coliform bacteria in the feces can be reduced to less than 1,000 organisms per gram of wet stool.

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* Read in the Section on Surgery, General and Abdominal, American Medical Association, Ninety-Eighth Annual Session, Atlantic City, June 8, 1949. Since this paper was submitted for publication, November, 1949, we have had the opportunity to evaluate "Combiotic" tablets, kindly prepared by Charles Pfizer and Co., Inc., which combine streptomycin sulfate 250 mg., bacitracin 5000 units, and polymyxin 20 mg., in preparation of the bowel for intestinal resection. Eight tablets a day, divided in 4 doses, to 20 patients, effected substantially the same results as obtained with the streptomycin-glucuronolactone combination, that is, maximal suppression was obtained in 36 to 72 hours. Prolonged administration of "Combiotic" tablets did not prevent the emergence of streptomycin-resistant bacteria. No other untoward effects were observed.

Intestinal obstructions, the presence of ulcerated lesions in the bowel, intestinal perforations, and intestinal fistulas, in general, interfere with the removal of susceptible bacteria from the intestinal tract, regardless of the antiseptic, or combinations of antiseptics, used.

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The sulfonamide drugs, however, have a number of disadvantages. Because large doses are necessary, toxicity as a result of absorption is always a possibility. The action of sulfanilamide and its derivatives is relatively slow. Finally, certain bacteria resident in the intestinal tract are refractory to them.

At least two factors limit the usefulness of penicillin as an intestinal antiseptic. When it is given orally, it is readily absorbed into the bloodstream from the upper digestive tract, while coliform bacteria, which dominate the fecal flora in the lower portion of the intestinal tract are either moderately or completely refractory to penicillin, or produce enzymes which inhibit or destroy its antibiotic action.

Streptomycin has numerous potential advantages over the sulfonamide drugs in intestinal surgery. It is not readily absorbed from the gastro-intestinal tract. Instead, it remains in the lumen of the bowel in high concentration. It is much more effective *in vitro* than the sulfonamides against coliform fecal flora. It does not irritate the intestinal mucosa. Finally, the results in the various clinics[3, 4] in which streptomycin has been used in preparation for resection of the colon indicate that it promptly effects a decrease in the bacterial flora, the number of *Escherichia coli* in the feces being reduced to less than 1000 colonies per gram of wet stool, within 48 to 60 hours after commencement of medication. With continued therapy, the suppression thus achieved may be maintained for five to eight days.

Like the sulfonamide drugs, however, streptomycin has its disadvantages. Its effect on coliform organisms appears to be only temporary and, regardless of the dosage used, the count can be expected to rise again after about five days. Moreover, the advantages of the rapid action of streptomycin are offset to a considerable extent by the development of drug resistance: After several days of treatment, there is frequently noted the emergence of an overgrowth of bacteria which are streptomycin-resistant. Lockwood[5] regards oral streptomycin as unreliable and does not recommend it for the preoperative preparation of surgical cases.

The effective suppression of fecal bacteria by chemotherapeutic and antibiotic methods was promptly found to result in the establishment of optimal conditions for the healing of operative wounds of the bowel.[6] It was also shown experimentally, and confirmed clinically, that the reduction of intestinal bacterial flora lessened the incidence of postoperative peritonitis, had an inhibitory effect on peritonitis which had already developed, and hastened the healing of ulcerations of the intestinal wall.

The emergence of drug-resistant bacterial strains, however, has remained a major problem in the application of chemotherapy and antibiotic therapy, and the investigation reported in this communication was undertaken with the idea of testing the effectiveness of supplementary agents in the prevention of this development.

MATERIALS AND METHODS

This investigation was carried out by administering to normal subjects and to subjects with disease of the large bowel streptomycin, both alone and

in combination with aluminum pectinate and glucuronolactone, according to a fixed routine. The effects of aureomycin, Chloromycetin, and of polymyxin were studied by the same plan.

Aluminum pectinate is a derivative of pectin, which is a hydrophilic colloid of great absorptive properties. Glucuronolactone, an inner anhydride of glucuronic acid, is a relatively stable crystalline substance, which forms spontaneously on dehydration of the acid. Glucuronic acid is normally conjugated in the liver with certain vitamins and sex hormones. It is also the principal agent by which such drugs as aspirin, morphine, camphor, chloral hydrate and the sulfonamides are detoxified in the liver. It is normally found in the blood and urine in conjugated forms. Both glucuronolactone and aluminum pectinate were supplied in two forms, in gelatin capsules containing 0.5 Gm., and in tablets already mixed with streptomycin. There was no observed difference in the activity of the two forms.

It is not yet clear why bacterial suppression of the feces is enhanced by either aluminum pectinate or glucuronolactone. We have no opinion about aluminum pectinate,[7] but are of the opinion that glucuronolactone may reduce the pH of the stool and possibly in this way impair the survival of bacteria.

No toxic reactions were observed from the ingestion of aluminum pectinate, glucuronolactone, streptomycin, or polymyxin, but aluminum pectinate produced fullness and bloatedness which were sometimes extremely annoying. Clinically, glucuronolactone is preferable to aluminum pectinate because it is less bulky, and acts more rapidly.

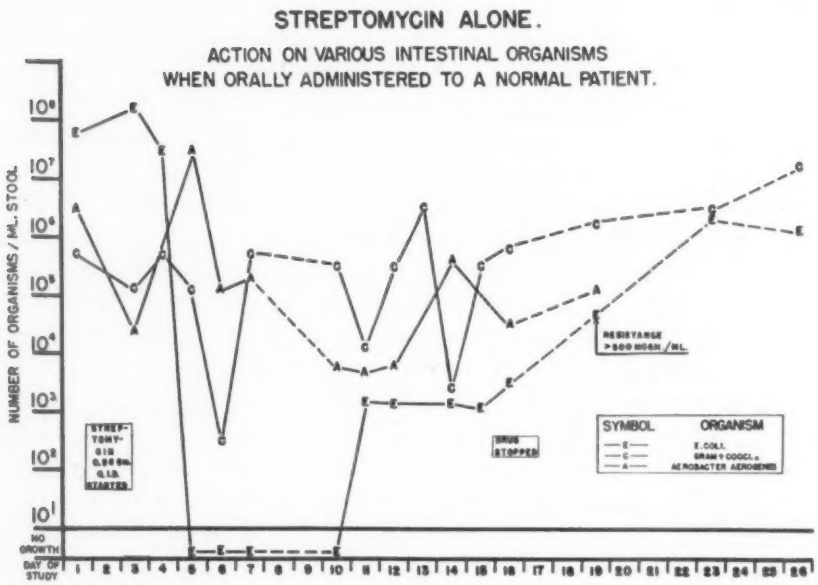
The laboratory procedure was as follows: A known weight of fresh stool, collected in a sterile box, was diluted 50 times in nutrient broth. The suspension was then serially diluted and 0.1 cc. of the diluent was streaked on agar containing blood, eosin methylene blue or sodium azide. Agar plates were incubated aerobically and sodium azide plates anaerobically. The sodium azide plates brought out gram-positive organisms and Bacteroides. Gram-positive organisms identified included hemolytic and nonhemolytic Streptococcus, Micrococcus and Clostridium. The gram-negative organisms included *Escherichia coli*, Proteus, Aerobacter and Pseudomonas. *Esch. coli*, Aerobacter, Streptococcus and Micrococcus were the only organisms present consistently and in sufficient numbers to use in the evaluation of the efficacy of drug action.

In addition to examination of the stools, as described, swabs were taken directly from the mucosa of the colon after resection and the material thus secured was planted on aerobic and anaerobic media. Postoperative bacteriologic studies were continued by the routine employed before operation.

RESULTS

Control Cases. Two healthy subjects were used as controls to furnish a base line for the effect of streptomycin alone on the fecal flora. Each was given 0.5 Gm. orally four times daily for 18 days. Results in both patients were essentially the same (Fig. 1). *Esch. coli* disappeared from the stools

FIG. 1


STREPTOMYCIN ALONE.
ACTION ON VARIOUS INTESTINAL ORGANISMS
WHEN ORALLY ADMINISTERED TO A NORMAL PATIENT.
NUMBER OF ORGANISMS / ML. STOOL
SYMBOL ORGANISM
E. COLI.
AEROBACTER AEROGENES
DRUG STOPPED
NO GROWTH
DAY OF STUDY

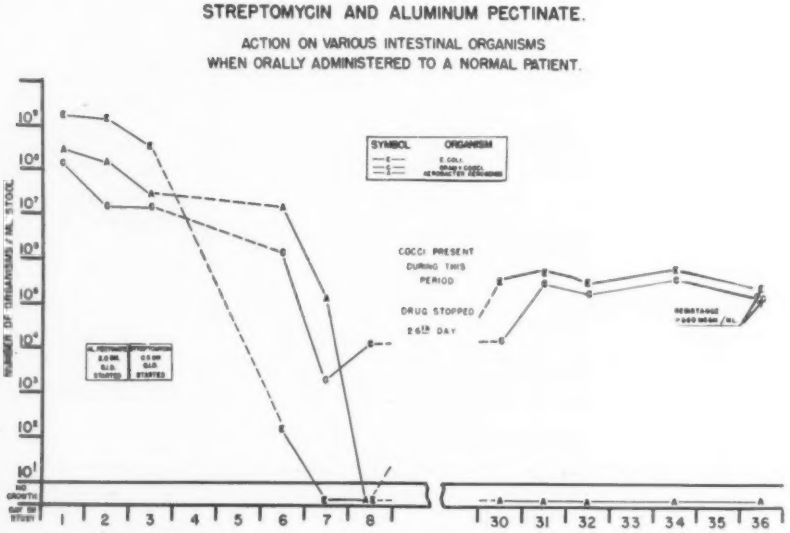

STREPTOMYCIN AND ALUMINUM PECTINATE.
ACTION ON VARIOUS INTESTINAL ORGANISMS
WHEN ORALLY ADMINISTERED TO A NORMAL PATIENT.
SYMBOL ORGANISM
COCCI PRESENT DURING THIS PERIOD
DRUG STOPPED 26TH DAY
NUMBER OF ORGANISMS / ML. STOOL
NO GROWTH
DAY OF STUDY

FIG. 2

within 48 hours. *Aerobacter aerogenes* and gram-positive cocci were not significantly depressed. Drug fast organisms occurred in both subjects six days after maximal suppression, in spite of continued administration of the drug.

Streptomycin-Aluminum Pectinate. Five normal subjects were given 0.5 Gm. of streptomycin combined with 2 Gm. of aluminum pectinate by mouth four times daily for 16 days. Results in all five cases were strikingly similar (Fig. 2). At the conclusion of treatment the stools were normal in color and had the consistency of a semi-gel while the fecal odor was diminished or absent. *Esch. coli* was completely suppressed within 24 to 60 hours after treatment had been begun. *A. aerogenes* (which was not uniformly present) disappeared at about the same time. Most strains of *Esch. coli* were streptomycin sensitive. Except for hemolytic streptococci, gram-positive cocci were not significantly reduced. Clostridium, Bacteroides and yeasts were also not materially affected. Neither *Esch. coli* nor *A. aerogenes* reccurred while therapy was continued, but the organisms which had been suppressed re-appeared, on the average, within 48 hours following the withdrawal of streptomycin.

Following this demonstration in normal subjects, six patients with various diseases of the colon were treated with streptomycin and aluminum pectinate by the routine described for four days before resection of the bowel. The last dose was given in each instance two hours before operation, through a Miller-Abbott tube which had been inserted the previous day. Other preoperative preparation consisted of a low residue diet, a dose of castor oil (2 ounces) two days before operation, and repeated enemas over the same period of time.

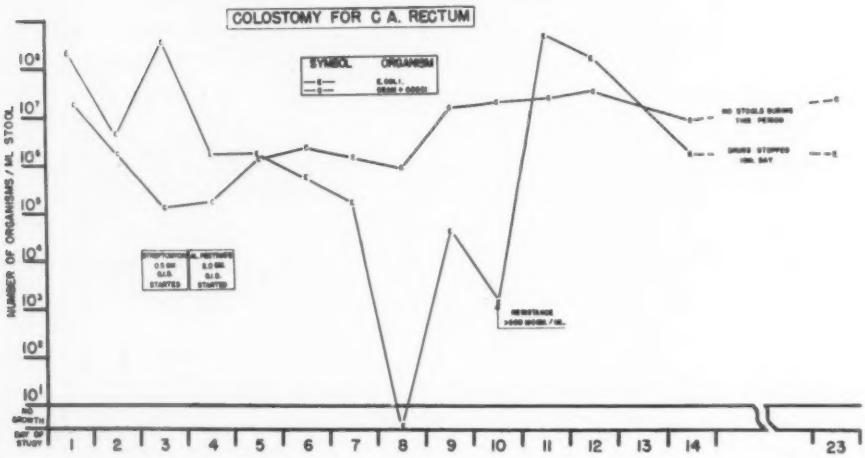
In four of the six patients, the response was satisfactory. *Esch. coli* and other gram-negative bacilli were suppressed within 60 hours, and there was also a significant reduction in the numbers of gram-positive cocci, particularly the hemolytic streptococci. Clostridium, Bacteroides and Monilia were unaffected. The operative procedure was greatly simplified because the bowel was soft, flat, and readily handled. How soon after operation organisms began to reappear in the feces is not known, since stools were not usually passed before the fourth postoperative day. A liquid specimen removed through the Miller-Abbott tube from the descending colon of one patient on the second postoperative day revealed streptomycin-sensitive *Esch. coli* in small numbers. In the other three cases in this group, the first stools showed a moderate growth of *Esch. coli,* most of which were streptomycin-sensitive.

The fifth patient had an annular carcinoma of the left colon which had caused serious obstruction and the sixth, who had a functioning colostomy, had multiple constrictions of the bowel caused by carcinomatosis (Fig. 3). In both instances, most of the *Esch. coli* found in the intestine were drug-resistant and the response to treatment was therefore poor.

The patient with the colostomy was not operated upon. The other five underwent resection of the colon, with open anastomosis. None developed

FIG. 3

STREPTOMYCIN AND ALUMINUM PECTINATE.
FAILURE TO SUPPRESS RESISTANT INTESTINAL ESCHERICHIA COLI AND GRAM POSITIVE COCCI WHEN ORALLY ADMINISTERED.



STREPTOMYCIN AND GLUCURONOLACTONE

ACTION ON INTESTINAL ORGANISMS OF A NORMAL PATIENT, DEMONSTRATING RE-INHIBITION OF ESCHERICIA COLI AFTER INTERRUPTION OF THERAPY

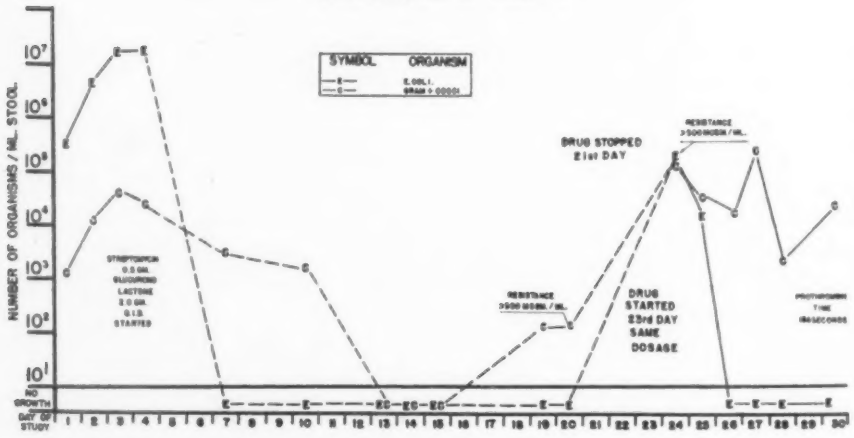


FIG. 4

peritonitis. Whether this fortunate outcome could be attributed to the preoperative therapy it is not possible to say, since all were given 100,000 units of penicillin by the parenteral route every eight hours after operation, for periods varying from seven to 14 days.

Streptomycin-Glucuronolactone. Eight normal subjects were given 0.5 Gm. streptomycin, combined with 2 Gm. of glucuronolactone, by mouth four times daily for 16 days in seven cases, and for 33 days in one case. In seven of the eight cases coliform bacteria were suppressed within 24 to 48 hours after the beginning of treatment (Fig. 4). In the eighth case *Esch. coli* was not eliminated until the seventh day. In all eight cases suppression was maintained for at least 48 hours after the drugs had been withdrawn. When re-growth occurred, *E. coli* were found to be streptomycin-fast. As to the other organisms, micrococci were reduced to some degree in all subjects and were completely, though temporarily, eliminated in four. Clostridium, Bacteroides and Monilia were unaffected, as were unidentified anaerobic gram-negative rods which were occasionally isolated. It may be that the same results could have been accomplished with a smaller dosage than 8 Gm. daily, but we have not yet carried out tests to determine this point.

Esch. coli re-appeared within 48 hours after treatment had been discontinued in the single case in which glucuronolactone and streptomycin were continued for 33 days. It grew in media containing 0.5 mg. of streptomycin per milliliter. When therapy was reinstituted, the organisms were again suppressed, the inhibition being maintained for another seven days. This course of events suggests that resistant organisms do not permanently dominate the fecal flora following the oral administration of streptomycin.

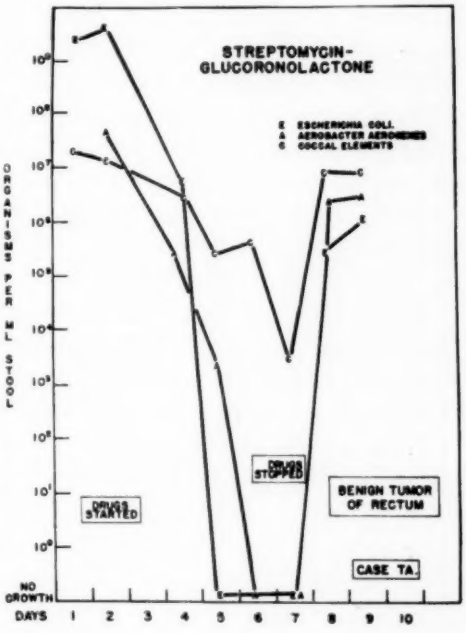


FIG. 5

After this trial in normal subjects, six patients with various lesions of the colon were treated with streptomycin and glucuronolactone by the routine described, for five days prior to resection of the bowel. In all six cases the response was satisfactory (Fig. 5). Susceptible coliform bacteria were suppressed in all instances, maximal suppression being attained in 60 hours in four patients, and by the fifth day of treatment in the other two. Cocci were inconstantly but significantly reduced in numbers and inactive Clostridia and Monilia

appeared unaffected. The time for achievement of maximal suppression, it should be noted, was longer than in the normal subjects.

Aureomycin and Chloromycetin. Aureomycin and Chloromycetin, which became available for study during the course of this investigation, were given to three and to two patients, respectively, in 0.5 Gm. dosages four times daily for 12 days. Gram-positive fecal bacteria were not affected, nor were gram-negative bacteria other than *E. coli.* The suppression accomplished was slight in comparison with that obtained with either sulfonamide drugs or streptomycin. Aureomycin, and Chloromycetin, at least in the dosages used in this study, therefore do not seem to offer much promise as intestinal antiseptics. Both antibiotics are rapidly absorbed into the blood when they are administered orally, but both apparently reach the lower digestive tract in bacteriostatic concentrations for some organisms.

Polymyxin B. This is derived from cultures of Bacillus polymyxa, and became available for testing in the course of this investigation. It is not absorbed from the gastro-intestinal tract, it exerts a rapid bacteriostatic action on many coliform bacteria as well as on certain strains of cocci, and on a weight and dosage basis it is many times more active against coliform organisms than is streptomycin. Proteus strains, in our experience, are indifferent to its action. Drug-fastness does not occur readily.

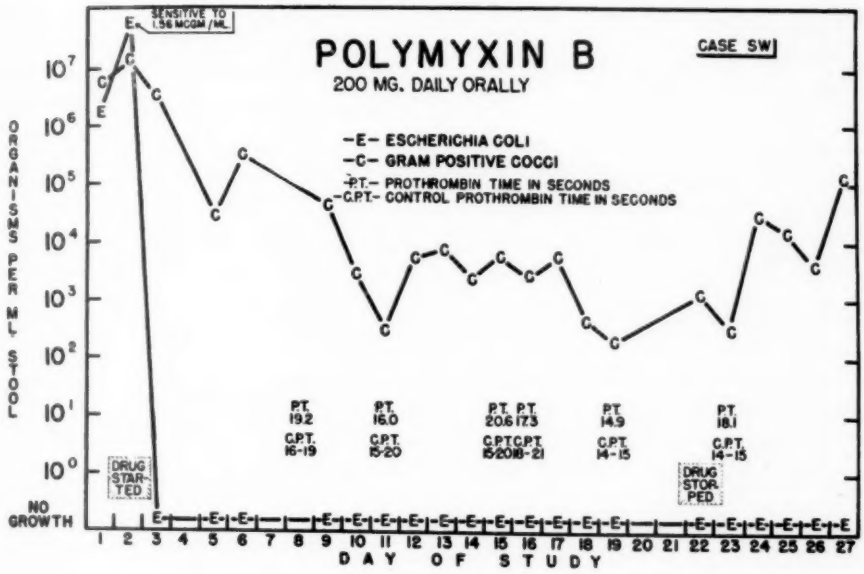
Polymyxin was given orally in divided doses four times daily to five patients who received 200 mg. a day (Fig. 6), and to seven patients who received 400 mg. per day. Treatment was continued for 16 days in the six subjects. Polymyxin was also given for five days to six patients with intestinal lesions (Fig. 7), as part of the preoperative regimen. All coliform organisms were suppressed within 24 to 60 hours after treatment had been begun and suppression was maintained for two days after it was discontinued. The minimally effective dosage appears to be 200 mg. daily. Proteus was present in four of the 12 patients, and eventually dominated the fecal flora. In two of these patients, no additional effects could be attributed to the concomitant administration of glucuronolactone with polymyxin. In each of two others, Proteus could not be recovered after two days of oral streptomycin therapy, 2 Gm. daily.

SUMMARY AND CONCLUSIONS

Tests in 24 normal subjects and in 20 patients with lesions of the colon demonstrate that streptomycin, in dosages of 0.5 Gm. four times daily, eliminates coliform bacteria from the feces at the end of two to four days' treatment. It cannot suppress fecal cocci, clostridia and yeasts and it inhibits Aerobacter only inconstantly. Because of emergence of drug-fast bacteria, maximal suppression can be maintained by streptomycin alone for not more than four to six days.

When glucuronolactone is given in combination with streptomycin, the period of suppression is lengthened to beyond 14 days or more. Aluminum

FIG. 6


POLYMYXIN B
200 MG. DAILY ORALLY
CASE SW
SENSITIVE TO 1.56 MCGM/ML
-E- ESCHERICHIA COLI
-C- GRAM POSITIVE COCCI
-P.T.- PROTHROMBIN TIME IN SECONDS
-C.P.T.- CONTROL PROTHROMBIN TIME IN SECONDS
ORGANISMS PER ML STOOL
NO GROWTH
DRUG STARTED
DRUG STOPPED
P.T. 19.2 C.P.T. 16-19
P.T. 16.0 C.P.T. 15-20
P.T. P.T. 20.6 17.3 C.P.T. C.P.T. 15-20 18-21
P.T. 14.9 C.P.T. 14-15
P.T. 18.1 C.P.T. 14-15
DAY OF STUDY

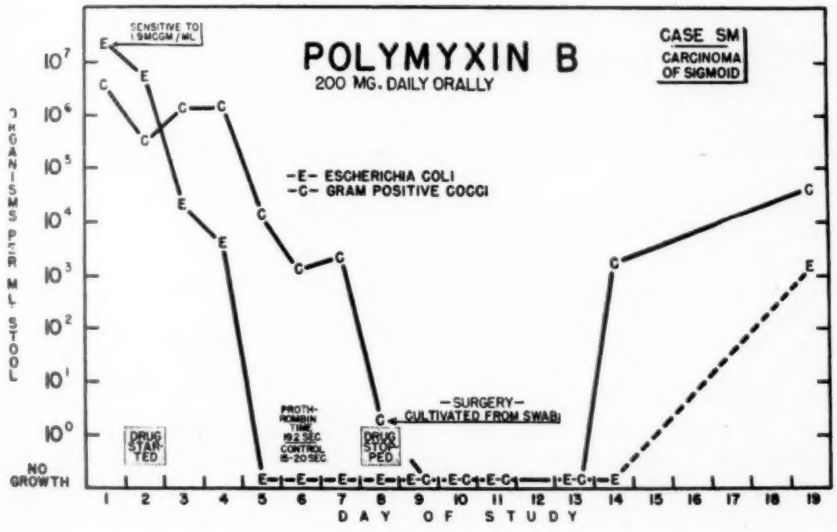

POLYMYXIN B
200 MG. DAILY ORALLY
CASE SM
CARCINOMA OF SIGMOID
SENSITIVE TO 1.5MCGM/ML
-E- ESCHERICHIA COLI
-C- GRAM POSITIVE COCCI
ORGANISMS PER ML STOOL
NO GROWTH
DRUG STARTED
PROTHROMBIN TIME 19.2 SEC CONTROL 15-20 SEC
DRUG STOPPED
-SURGERY-
CULTIVATED FROM SWAB
DAY OF STUDY

FIG. 7

pectinate with streptomycin gives less consistent responses than the glucuronolactone-streptomycin combination.

Polymyxin B, in total daily dosages of 200 to 400 mg., eliminates all coliform bacteria except Proteus from the feces as rapidly as streptomycin. Aureomycin and chloromycetin in daily doses of 2 Gm. a day do not appear promising as agents for the preoperative preparation of surgical cases.

Regardless of the type of chemotherapeutic treatment used, maximal suppression of intestinal bacteria occurs 24 to 48 hours later in patients with lesions of the colon than in normal subjects.

The successes of antiseptic measures in the suppression of the bacterial flora of the large intestine must not blind the surgeon to the fact that this form of therapy is only one of several measures responsible for the recently reported reduction in the mortality and morbidity of surgery of this part of the intestinal tract. Replacement therapy, including massive blood transfusion, and intestinal decompression have played at least as important a part in this fortunate outcome.

The aluminum pectinate and glucuronolactone used in this investigation were kindly supplied by the Commercial Solvents Corporation, and the polymyxin by Burroughs Wellcome and Company.

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NOTE: See letter to editor on page 319 for a discussion of this article.

PENICILLIN AND STREPTOMYCIN IN THE TREATMENT OF EXPERIMENTAL *ESCHERICHIA COLI* PERITONEAL INFECTION*

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In the management of peritonitis, antibiotic therapy has been generally regarded as a factor of definite importance in the reduction of mortality. The impression appears to be prevalent that penicillin in large dosage is the drug of choice, in spite of the fact that the common perforative or bowel-contamination type of peritonitis represents a multi-bacterial invasion of the peritoneal cavity, in which gram-negative bacilli of the coliform group predominate, estimates of the incidence in man ranging from 65 per cent[3] to 77 per cent[15] to 87 per cent.[17] Streptomycin, recognized as highly effective against gram-negative organisms, has failed to achieve a place of prominence in therapy in peritonitis and has been assigned to a definitely subsidiary role.

HISTORICAL

In the etiology of secondary peritonitis, which represents an infection enhanced in severity by reason of the synergistic effect of the invading bacteria, it is difficult to identify the primary offender. The role of *Escherichia coli,* which was the organism used in this experimental study, in the production of peritonitis has been the subject of a vast difference of opinion. The confused state of thought regarding the etiology of peritonitis is readily apparent in the historical portion of a report by Bower, *et al.*,[3] on the bacteriology of spreading peritonitis. Meleney, *et al.*,[18] emphasized the importance of synergism of bacteria in the production of peritonitis and concluded that *E. coli* was more virulent than *Streptococcus anhemolyticus* or *Clostridium welchii.* Owen[28] found that the coliform group were the only intestinal bacteria which were consistently pathogenic in producing peritonitis. Altemeier[1] recognized the importance of bacterial synergism in enhancing pathogenicity, and was unimpressed with the invasive qualities of *E. coli* alone. In advocating large doses of penicillin for clinical peritonitis, Crile[6] emphasized the primary role of gram-positive cocci and depreciated the importance of coliform bacteria. Farris and Romack[8] expressed an opposite opinion, designating the intestinal streptococci as essentially nonpathogenic except for their reinforcing effect upon *E. coli.*

* The authors wish to acknowledge with gratitude the help and suggestions of Dr. Warren H. Cole in this study. The expense of these experiments was partly defrayed by a grant from Abbott Laboratories, Chicago, Illinois. Submitted for publication August, 1949.

Experimental peritonitis, for the evaluation of penicillin and streptomycin therapy, has in the main been produced by some modification of the Bower technic,[4] constituting in brief a ligation of the blood supply and base of the appendix at the time of celiotomy, and subsequently stimulating the bowel motility with castor oil, thereby producing an infection which simulates clinical peritonitis. This method has the disadvantage of instituting a multiple and variable bacterial infection, in the course of which it is impossible to identify the specific action of a therapeutic agent upon any single one of the multiple invaders. Fauley, *et al.*,[9] noted excellent results in a series of dogs with experimental peritonitis produced by this method and treated with penicillin. The results of experimental studies with similar technics on dogs are, in the main, quite favorable to the use of penicillin and definitely unfavorable to the use of streptomycin, at least when used alone, according to the reports of Murphy, *et al.*,[22] Zintel,[37] Silvani, *et al.*,[31] and Rothenberg, *et al.*[29] Farris and Romack,[8] applying the Bower technic to rabbits, noted excellent results with streptomycin therapy. The marked difference in results with streptomycin therapy in dogs and in rabbits may possibly be related to the absence of an anaerobic intestinal flora in the latter. Minimal investigative work has been reported on experimental peritonitis produced by a single type of bacteria, and this has been in connection with an evaluation of sulfonamide therapy by Cooper, *et al.*,[5] and by Klinefelter.[13, 14]

THE ROLE OF MUCIN

The technic of suspending bacteria in a mucin preparation for intraperitoneal injection was adopted for the production of peritonitis in this experimental study. The phenomenal effect of mucin[19, 20, 23, 24] in enhancing bacterial invasion is well known, but its exact mode of action is far from clear.[27] When bacteria are injected into the peritoneal cavity of an experimental animal, even in fairly large numbers, they are usually quite promptly absorbed into the blood stream and destroyed; apparently very little active proliferation of the organisms occurs. However, when mucin is present, the initial bacteremia is minimal and transitory; the bacteria, following a short lag period, proliferate profusely and establish a focus of infection, from which source a bacteremia reappears and usually progresses to a fatal termination. The volume, concentration, and physical characteristics of the mucin preparations are of importance in affecting its action.[16, 24] Mucin does not appear to act primarily as a culture medium for intraperitoneal growth.[12, 16, 20] The virulence of bacteria is not permanently increased by exposure to mucin *in vitro*[24] or *in vivo*.[10] Authors appear to favor the concept that the action of mucin represents a temporary depression of, or interference with, the natural defenses of the host against invasion.[16, 20, 25] This may occur through the mechanism of the formation of a protective coating of bacteria by the mucin,[34] through limitation of phagocytosis or intraphagocytic digestion,[16, 24] through the retardation of a prompt migration of phagocytes into the peritoneal cavity,[7]

through a depression of the action of immune bodies in the serum,[12, 16, 26] or through some mechanism as yet unknown. The salient feature from a practical point of view appears to be that, by reason of the presence of mucin, bacteria are enabled to survive during the initial critical period, so that a focus of active infection is established within the peritoneal cavity.

MATERIALS AND METHODS

A method of producing a lethal *E. coli* peritonitis in white mice, about 20 Gm. in weight, by the intraperitoneal injection of bacteria suspended in mucin was developed and standardized. The strain of *E. coli** was isolated from a clinical case of intestinal obstruction. Powdered granular mucin† was sterilized by autoclaving and was subsequently suspended in sterile physiologic saline solution. This method caused less alteration in the physical characteristics of the mucin than did the method of autoclaving a suspension of the mucin, and was consequently preferred. The bacteria, grown on agar slants, were suspended in physiologic saline solution in a concentration controlled turbidimetrically. Equal volumes of bacterial suspension and of 5 per cent mucin were thoroughly mixed and 0.5 cc. of the coli-mucin mixture was administered intraperitoneally, the inoculum representing approximately 50 bacteria in a final mucin concentration of 2.5 per cent, unless otherwise indicated. In order to obviate the necessity of carrying cultures on artificial media with the possibility of a decrease in virulence, as occurred during the preliminary phases of the experiment, and in order to give assurance that an organism of the same characteristics as the original would be used throughout the experiment, a large number of broth cultures of the original strain in small tubes were kept frozen at minus 30° Centigrade; from this source agar slants were inoculated as needed.

A postmortem examination of the peritoneal cavity was made of all mice succumbing to the infection; a smear of the peritoneal exudate was made and stained by Gram's method, and a tube of Brewer's thioglycolate medium as well as an Endo's plate were inoculated with peritoneal exudate. If the foregoing indicated the presence of *E. coli*, the recovered bacteria were presumed to be the injected organisms, and the cause of death. Periodically, in the initial stages of the work, the cultural characteristics of the recovered bacteria were compared with the original and found to be identical, thereby establishing confidence in the technic. Contamination of the peritoneal cavity was minimal and occurred infrequently, provided the examination was made reasonably soon after death. In those animals which died during the night and

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* Characteristics of this organism: fermentation of glucose, sucrose, mannitol, lactose, and dulcitol occurred with the production of acid and gas; the Voges-Proskauer reaction was negative; the methyl red reaction was positive; indole production was positive; citrate utilization was negative; urease reaction was negative for NH_3; the bacterium was motile.

† Granular Mucin, Type 1701-W, Wilson Laboratories.

were examined during the following morning small numbers of contaminants were frequently present, but they were ignored after observation identified them as representing merely postmortem invasion of the peritoneal cavity.

Solutions of the antibiotic drugs in physiologic saline solution were used for treatment of the animals; the slow absorption type preparations of penicillin were avoided in order to maintain the drugs on a comparable basis. In the series of animals treated subcutaneously, the initial treatment of the infected animals was administered as soon after the intraperitoneal inoculations as practicable, usually within one hour. The treatment was repeated in approximately 12 and 24 hours. Some animals succumbed prior to completion of the course of therapy. In the series of animals treated intraperitoneally, a single injection of the drug was administered soon after the intraperitoneal inoculation of the bacteria in mucin, and no further therapy was given.

In the main, untreated animals died in 18 to 24 hours. Effective and consistent prolongation of the survival time was not achieved by reduction in the numbers of bacteria injected, nor by a decrease in the volume or the concentration of the mucin suspension. Since the survival time was of short duration, it was eliminated as a criterion of evaluation of therapeutic results, and conclusions were drawn solely from the mortality percentages. However, it appeared that the survival period of animals succumbing in the various treatment categories varied inversely with the eventual mortality of the group.

RESULTS

The remarkable effectiveness of mucin in enhancing bacterial invasion is readily apparent from a simple comparison. Though the minimal lethal dose of the strain of *E. coli* was not determined when the bacteria, suspended in physiologic saline solution, were injected intraperitoneally, animals were observed to withstand approximately 6,000,000 bacteria without visible deleterious effect. In contrast, mice injected with the coli-mucin suspension, using approximately 50 bacteria per mouse, showed a mortality of 97.6 per cent.

The *in vitro* sensitivity of the strain of *E. coli* to the antibiotic drugs was determined by the method of Vicher and Levinson.[35] Bacterial growth was evident in broth at a penicillin concentration of 100 units per cc., and absent at 120 units per cc. Similarly, growth was noted in broth at a streptomycin concentration of 0.004 mg. per cc., and absent at 0.008 mg. per cc. Since these tests were made with serial dilutions of the antibiotics from regular clinical vials, without assay of the concentrations against standard antibiotic solutions, the above figures represent a range of sensitivity rather than precise values.

1. *Effect of subcutaneous therapy.* Mice, which had received the standard intraperitoneal inoculation of 0.5 cc. of the coli-mucin suspension of approximately 50 bacteria per mouse, were treated with varying dosages of penicillin and streptomycin, administered subcutaneously twice a day for a total of three injections, with results as recorded in Table I.

The effectiveness of both antibiotic drugs against the gram-negative infection was readily apparent, provided the dosage was adequate. In order to visualize more clearly the vast difference in size of the dosage of the two drugs used, note that, if the effective daily dosage of 40,000 units of penicillin and 0.2 mg. of streptomycin are transposed on a weight basis from a 20 Gm. mouse to a 60 Kg. individual, they become respectively 120,000,000 units

TABLE I.—*Effect of Subcutaneous Antibotic Therapy in Experimental Peritonitis.*

PENICILLIN*	Controls	1000 U	2500 U	5000 U	10,000 U	15,000 U	20,000 U
No. mice	54	10	20	27	22	22	29
Mortality	93%	100%	80%	78%	43%	36%	0%

STREPTOMYCIN*	Controls	0.01 mg.	0.05 mg.	0.1 mg.
No. mice	31	23	25	35
Mortality	100%	87%	44%	3%

* The dosage listed was given subcutaneously three times: the first at the time of injection of bacteria; the second and third were given approximately 12 and 24 hours later, respectively.

of penicillin and 0.6 Gm. of streptomycin for the human being. Admittedly, weight alone is not an adequate basis of comparison; however, the comparison tends to aid in achieving an appreciation of the tremendously large dosage of penicillin and the comparatively small dosage of streptomycin required to control the infection.

TABLE II.—*Effect of Combined Penicillin and Streptomycin Therapy.*

Dosage*		Number	Experimental	Calculated Additive
Penicillin	Streptomycin	of Mice	Survival Rate	Survival Rate†
1,000 U	0.01 mg.	13	15%	13%
1,000 U	0.05 mg.	13	46%	56%
2,500 U	0.01 mg.	13	8%	33%
2,500 U	0.05 mg.	13	92%	76%
5,000 U	0.01 mg.	16	44%	35%
5,000 U	0.05 mg.	16	87%	78%
10,000 U	0.01 mg.	12	100%	70%

* Administered subcutaneously as in Table I.
† Calculated from Table I.

2. *Effect of combined penicillin and streptomycin therapy.* With the concept in mind that perhaps small amounts of streptomycin might increase the susceptibility of *E. coli* to penicillin, so that the effective level of penicillin therapy might be reduced, various combinations of the drugs were tested on animals prepared identically with those in the previous experiment. The results are summarized in Table II.

The calculated additive survival rate, representing the total survival rate of the two drugs when used singly, were compared with the experimental survival rate in the combined therapy series. With the exception of group three, the results were fairly consistent, and tend to indicate that the combined use of the two drugs produced an additive, but not a synergistic effect. This conclusion was disappointing in that it failed to substantiate the premise

which prompted this series of experiments; however, the fact that the two drugs have an additive effect and can be used together without antagonistic action is a conclusion of considerable practical importance.

3. *Effect of increasing the number of bacteria.* Maintaining other factors constant, the previously determined protective dosages of the drugs were then challenged by increasing the number of bacteria injected. The results of injecting 50, 5000, and 500,000 organisms per mouse are recorded in Table III.

TABLE III.—*Effect of Increasing the Numbers of Bacteria.*

PENICILLIN*			
20,000 U	50 Coli	5,000 Coli	500,000 Coli
No. mice	29	14	14
Mortality	0%	57%	79%
STREPTOMYCIN*			
0.1 mg.			
No. mice	35	14	23
Mortality	3%	21%	87%

* Administered subcutaneously as in Table I.

Though the numbers of animals were relatively small, the trend was clear cut, and it was obvious that previously protective dosage levels were grossly inadequate when confronted with the invasion of large numbers of bacteria. The comparative mortalities with penicillin and streptomycin, using 5000 coli, reflected disadvantageously against penicillin.

4. *Effect of therapy against large numbers of bacteria.* Tests were next conducted to determine the effectiveness of the drugs in progressively increas-

TABLE IV.—*Effect of Therapy Against Large Numbers of Bacteria**

PENICILLIN†						
	Controls‡	20,000 U		60,000 U		100,000 U
No. mice	20	14		23		17
Mortality	95%	78%		43%		53%
STREPTOMYCIN†						
	Controls‡	0.1 mg.	0.5 mg.	1.0 mg.	2.5 mg.	5.0 mg.
No. mice	25	23	23	24	24	24
Mortality	100%	87%	74%	46%	12.5%	12.5%

* 500,000 organisms per mouse.
† Administered subcutaneously as in Table I.
‡ Controls received the standard 50 E. coli inoculum.

ing subcutaneous dosage against a challenge of the 500,000 range of bacteria in mucin. The extreme severity of this test is readily appreciated in the light of the fact that it represents a 10,000 fold increase over the inoculum of 50 organisms in the control series of 128 animals, which exhibited the high mortality of 97.6 per cent. The results are summarized in Table IV.

The dosage of 100,000 units of penicillin was definitely in the toxic range, since animals receiving this dosage without the coli-mucin suspension showed a 33 per cent mortality. The lowest mortality of 12.5 per cent in this experiment achieved with the relatively large dosages of 2.5 mg. and 5.0 mg. of

streptomycin twice a day for a total of three injections may be regarded as fairly satisfactory in view of the extreme severity of the infection.

5. *Effect of Intraperitoneal therapy.* In an attempt to simulate a clinical situation of peritoneal contamination during a surgical procedure on the gastro-intestinal tract, when the antibiotic drugs might advantageously be used for their local prophylactic effect in the abdominal cavity, mice were inoculated intraperitoneally with the standard coli-mucin suspension, using about 50 bacteria; within an hour they were treated with a single intraperitoneal injection of the drug. This therapy was not supplemented with subcutaneous administration of the drugs. The results are recorded in Table V.

In the series of animals treated intraperitoneally, the superiority of streptomycin over penicillin was still more evident than in the animals treated subcutaneously. Even the 20,000 unit dosage of penicillin failed to render complete protection. On the other hand, one-half of the comparable dosage of 0.1 mg. of streptomycin, namely 0.05 mg., effectively prevented a single

TABLE V.—*Effect of Intraperitoneal Therapy.*

PENICILLIN*					
	Controls	2000 U	5000 U	10,000 U	20,000 U
No. mice	41	23	27	29	27
Mortality	95%	87%	41%	14%	15%
STREPTOMYCIN*					
	Controls	0.01 mg.	0.025 mg.	0.05 mg.	0.1 mg.
No. mice	40	26	28	26	15
Mortality	97.5%	38%	7%	0%	0%

* One injection of the dosage listed was given intraperitoneally soon after inoculation of the bacteria.

fatality, and one-quarter of the dosage of 0.1 mg. of streptomycin, namely 0.025 mg., gave a mortality of 7 per cent, a value which is one-half of the lowest mortality achieved in the penicillin series.

The intraperitoneal injection of streptomycin was found to be more effective than the subcutaneous administration. A total of 0.3 mg. of streptomycin, administered in three subcutaneous injections, resulted in a mortality of 3 per cent (Table I); a single injection of 0.05 mg. of streptomycin given intraperitoneally (1/6 of the subcutaneous dosage) resulted in no mortality (Table V), and a single injection of 0.025 mg. (1/12 of the subcutaneous dosage) gave a mortality of only 7 per cent (Table V).

The peritoneal cavities of animals treated intraperitoneally with the antibiotic drugs gave no indication of any deleterious effect as a consequence of the direct injection of the medication.

STUDY OF THE PERITONEAL EXUDATE OF THE EXPERIMENTAL MICE

A study of the peritoneal exudate yielded some significant findings. Grossly, the exudate showed considerable variation in quantity, viscosity, and turbidity, and no definite correlation appeared to exist between the characteristics of the exudate and the time of death, treatment or absence of treat-

ment, or mode of administration. Unless the animal had been dead for some time and postmortem change had occurred, the exudate was not malodorous. In general, Gram stains of the peritoneal exudate of untreated animals revealed innumerable gram-negative pleomorphic rods, and a variable number of peritoneal defense cells, some of which were readily identified as to type of cell, while others were in varying stages of disintegration, which precluded accurate identification. Polymorphonuclear leukocytes appeared to predominate. The pleomorphic character of *E. coli* should receive emphasis. Not only did the individual bacteria vary in the same culture from small, almost coccoid forms to larger, definite bacilli, but the appearance was further altered on different culture media, and within the peritoneal cavity. The

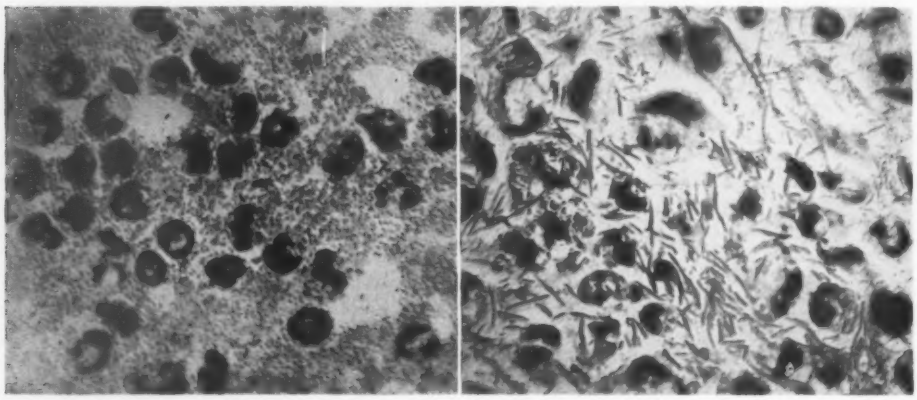

FIG. 1 FIG. 2

FIG. 1.—Peritoneal exudate of an untreated mouse. Note the phagocytic cells and the large numbers of *E. coli*.

FIG. 2.—Peritoneal exudate of a mouse treated with inadequate dosages of penicillin. Note the marked change in size and appearance of the bacteria as compared with Figure 1.

morphologic transformations induced *in vivo* as a consequence of certain conditions of antibiotic therapy seemed incredible when first noted.

Figure 1 is a photomicrograph made from a Gram stain of the peritoneal exudate of an untreated animal, No. 654. The large number of *E. coli* present and also the cellular response of the host are apparent. Figure No. 2, taken from a slide of the peritoneal exudate of a mouse, No. 800, which had received grossly inadequate treatment, namely 2500 units of penicillin subcutaneously (Table I), illustrates an extreme type of alteration in bacterial morphology as a consequence of the presence of low concentrations of penicillin. Prompt reversion to usual morphology occurred when these bacteria were returned to artificial media. Most of the peritoneal smears of the animals in this treatment category of 2500 units of penicillin exhibited similar changes in some degree; the relative numbers of large and small forms varied considerably throughout this series, and even the smaller forms were considerably larger than those in

the smears of untreated animals. Figure No. 3, taken from a smear of the peritoneal exudate of a mouse, No. 492, which had received 10,000 units of penicillin subcutaneously (Table I), presents an entirely different picture: comparatively few bacteria remain, these approximate the usual morphologic appearance, and both bacteria and cells appear poorly defined and give an impression of having sustained injury. The results in the 5000 unit penicillin series (Table I) were intermediate between the two preceding categories; far fewer bizarre forms were present than in the 2500 unit series, and many more bacteria than in the 10,000 unit group. In fact, atypical forms were noted in scattered fashion throughout the penicillin series. In the higher dosage treatment categories, it is possible that these atypical forms developed at some time before death when the penicillin concentration had fallen to a low level, comparable to the level in the 2500 unit series, which showed the phenomenon quite consistently.

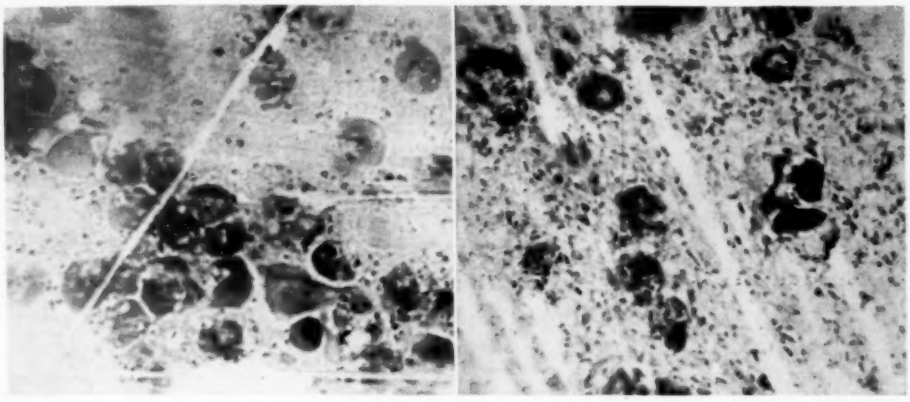

FIG. 3 FIG. 4

FIG. 3.—Peritoneal exudate of a mouse treated with larger doses (e.g., 10,000 units) of penicillin. Only a few bacteria remain and the bizarre forms present in Figure 2 are absent.

FIG. 4.—Peritoneal exudate of a mouse treated with streptomycin, showing a minor morphologic change. Note an increase in size of the bacilli as compared with Figure 1. The bizarre bacterial forms noted in Figure 2 are absent.

The phenomenon of bizarre morphologic change of the bacteria was singularly absent in the smears of the peritoneal exudate of animals treated with streptomycin. A few of the smears of the peritoneal exudate of the streptomycin series showed minimal changes in the bacteria, chiefly a slight increase in size. Figure No. 4, taken from the slide of the peritoneal exudate of the only animal, Mouse No. 511, which succumbed in the 0.1 mg. streptomycin group (Table I), illustrates the increase in size of the bacilli as compared with the bacteria in Figure 1. It is questionable that these minimal changes are fundamentally comparable to those noted with penicillin, but they are reported, since they represent some deviation from the findings in untreated animals.

DISCUSSION

The use of mucin to enhance the effectiveness of *E. coli* in the production of a high mortality is admittedly an artificial measure under the conditions of this experimental study. However, it should be pointed out that in the usual course of perforative peritonitis, mucin is available from the gastro-intestinal tract to accompany the bacteria, and perhaps in some manner to facilitate their invasion and protect them against the natural defenses of the body. By whatever mechanism the mucin acts, the infection inaugurated with it is overcome by an effective concentration of the antibiotic drug.

The phenomenon of bizarre morphologic transformation as a consequence of low dosage of penicillin is interesting. Similar changes have been reported by many investigators in *in vitro* studies.[2, 11, 30, 33, 36] Alture-Werber, *et al.*,[2] were attracted to this problem when some unusual fungoid forms were noted in the urine of patients under treatment with penicillin for urinary tract infection; these were judged to be atypical forms of *E. coli*. The phenomenon probably represents an inhibition of the process of reproduction of the bacteria by sublethal concentrations of penicillin. Survival with growth takes place, but sufficient interference with cellular metabolism has occurred so that there is a failure of fission. In the higher dosage range this effect is not observed since the antibiotic has a more completely inhibitory or lethal effect upon the bacteria. This concept of inhibitory action of antibiotic drugs directly upon bacteria *in vivo* in a manner similar to the inhibition of growth of bacteria in *in vitro* studies appears to agree with current evidence; however, a host protection factor is indicated in the demonstration by C. Miller, *et al.*[21] that protection of mice against the toxemia resulting from the injection of the endotoxins of various types of gram-negative bacilli was possible by prior intraperitoneal injection of penicillin.

In general, the impression was gained in the course of the experimental study that penicillin was not so consistent in its behavior as was streptomycin, and the question was raised whether a drug, assayed for potency with a gram-positive coccus, might not contain in different lots variable components of action with reference to activity against a gram-negative rod. No study in regard to this possibility was carried out. The findings of Rothenberg, *et al.*,[29] reported after these observations were made, relative to the superior effectiveness of penicillin preparations having a 15 to 25 per cent content of penicillin X over regular penicillin G tend to lend credence to the observation.

The effectiveness of large doses of penicillin in this experimental pure-culture coliform infection suggests the possibility that the favorable clinical results in treating secondary peritonitis with penicillin may proceed from a direct inhibiting action upon the gram-negative bacteria as well as from the control of the gram-positive coccus component of the inflammatory process. If the concept is valid that secondary peritonitis is a multi-bacterial infection, potentiated by reason of the synergism of the participating organisms, then it would appear logical, in view of the greater effectiveness of streptomycin

against gram-negative organisms of the coliform variety, to combine penicillin and streptomycin therapy in order to press the attack against the variety of invading bacteria at as many vulnerable points as possible.

CONCLUSIONS

1. Penicillin and streptomycin were both effective in controlling experimental *E. coli* peritoneal infections in mice, although streptomycin was more effective than penicillin. The dosage of streptomycin required to control the infection was comparatively much lower than that of penicillin.

2. Penicillin and streptomycin had an additive, but not a synergistic effect, when used in combined therapy in this experimental infection.

3. A direct relationship existed between the numbers of infecting bacteria and the size of the dosage of antibiotic drug required.

4. A single injection of streptomycin, given intraperitoneally, was remarkably effective in the control of intraperitoneal contamination by *E. coli.*

5. Bizarre morphologic changes in *E. coli* were noted *in vivo,* apparently as a consequence of sublethal concentrations of penicillin. Similar changes were not noted with streptomycin.

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THE CONSERVATIVE TREATMENT OF SALPINGITIS COMPLICATING MYOMATA UTERI*

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At Harlem Hospital, salpingitis is a frequent complication of other types of pelvic disease. One-third of the predominantly Negro patients, who are admitted with myomata uteri have coincidental pelvic inflammatory disease. Torpin found this incidence to be 54 per cent.[2]

Surgical treatment of salpingitis is rare in private practice because of the efficacy of conservative and antibiotic therapy. Barrows and Labate,[3] and Douglas,[4] have shown that sulfonamides are effective only if begun within five days of the onset of the primary attack of gonorrheal salpingitis. In city hospitals, patients often are hospitalized much later, frequently with palpable masses on admission. Chemotherapy and antibiotic therapy are of little or no value in such patients; consequently 20 per cent still require surgery for persistent symptoms or economic disability due to recurrent attacks.[5,6] J. T. Williams,[7] and H. E. Miller,[8] have had similar experiences.

The usual operation for salpingitis is bilateral salpingectomy or salpingo-oophorectomy. An analysis of the results of salpingectomy revealed an unsatisfactory mortality, postoperative morbidity and re-operation rate.[9-11] Interference with the ovarian blood supply, often requiring primary sacrifice of an ovary, has been a major objection to salpingectomy. C. Jeff Miller stated that one or both ovaries were removed in 70 per cent of women undergoing salpingectomy.[15] Furthermore, the re-operation rate for symptomatic cystic ovaries and/or bleeding from the retained uterus, following bilateral salpingectomy, is from five to ten per cent. As a result, most gynecologists defer surgery for inflammatory disease as long as possible, but when operation is indicated prefer hysterectomy and bilateral salpingectomy as the operation of choice.[10]

The danger of this radical procedure to the patient with inflammatory disease is reflected in the primary mortality rate quoted in the literature as ranging from 4.1 to 18.4 per cent.[6]

Although it is generally assumed that chemotherapy and antibiotics have lessened this mortality rate, the recent literature is lacking in definite statistics. H. E. Miller[8] in his comparative analysis of all types of surgery for pelvic inflammatory disease as contrasted with the statistics of his predecessor C. Jeff Miller, found a decrease in mortality rate from 2.5 per cent to 0.75 per cent. This improvement was not attributed by him to chemotherapy, but to

* Submitted for publication, July, 1949.

improved pre- and postoperative care, liberal use of blood transfusion, and the institution of a trained resident system. It is nevertheless significant, that of the 16 surgical fatalities reported ten occurred in cases on whom hysterectomy with salpingectomy were performed.

Since 1934, at Harlem Hospital bilateral cornual resection has been used as the operation of choice for the treatment of recurrent salpingitis. The concepts underlying the operation of cornual resection are based on bacteriologic and histo-pathologic evidence showing that gonorrheal infection from the endocervix reaches the tube by direct extension along the epithelium of the endometrium and endosalpinx. Interruption of this epithelial continuity by bilateral cornual resection prevents re-infection from the cervix ascending to the tube. It has been clearly shown that the tube does not re-infect itself.[13] On resolution of the existing inflammation in the retained tube, since re-infection cannot occur, cornual resection results in cure.

In 1940, 400 cases of cornual resection were presented without an operative fatality. A four-year follow-up of 286 of these cases revealed a clinical cure in 85 per cent, and all but three patients were restored to a full economic range of activity.[6] A similar study has been extended to 1000 cases of cornual resection with parallel results.[14] Only two patients have required re-operation for symptomatic cystic disease of the ovaries.

Hysterectomy for uterine disease, leaving behind infected tubes, is in essence similar to cornual resection, since it interrupts the epithelial continuity of the tube with the infected cervix. Accordingly, when fibroids and pelvic inflammatory disease are co-existent, hysterectomy, leaving the tubes and ovaries in situ, has been performed for the following reasons:

1. To preserve ovarian function in the young woman.
2. To diminish postoperative morbidity and intestinal injuries.
3. To reduce operating time, permitting a higher percentage of total hysterectomies.
4. To reduce operative mortality where separation of adnexae adherent to adjacent structures adds increased technical difficulties.

Curtis,[5, 16] who expounded the radical operation, nevertheless made modest concessions to his convictions as to the etiology and course of gonorrheal salpingitis. To preserve a normal ovary he did not hesitate to leave a healed, previously inflamed tube behind, "even when there was mild hydrosalpinx."

CLINICAL MATERIAL

This paper is based on an analysis of 135 consecutive cases operated upon in Harlem Hospital from January, 1943, to January, 1947. The group represents patients on whom hysterectomy was performed for uterine fibroids complicated by inflammatory adnexal disease, where one or both tubes and ovaries were left in situ.

The adnexae were not removed regardless of increased size or inflamed appearance at operation. However, if ovarian or tubo-ovarian abscess, or severe cystic disease of an ovary were present, salpingo-oophorectomy was performed.

Age. The youngest patient was 23, and the oldest 49 years of age. It is apparent that the majority (114 cases) were under 40 years, making ovarian salvage desirable (Fig. 1).

Symptoms.

Pain	127 cases
Metro-menorrhagia	85 cases
Urinary (frequency, urgency, dysuria)	42 cases
Leukorrhea	48 cases

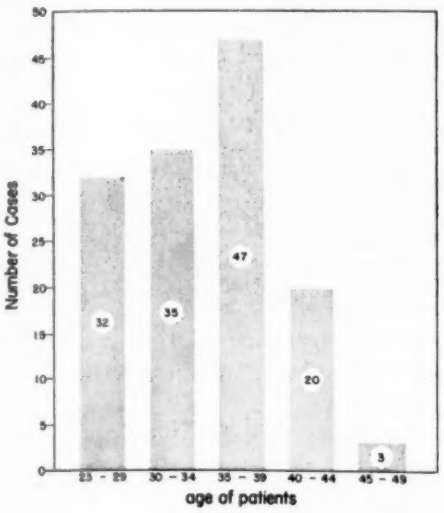

FIG. 1

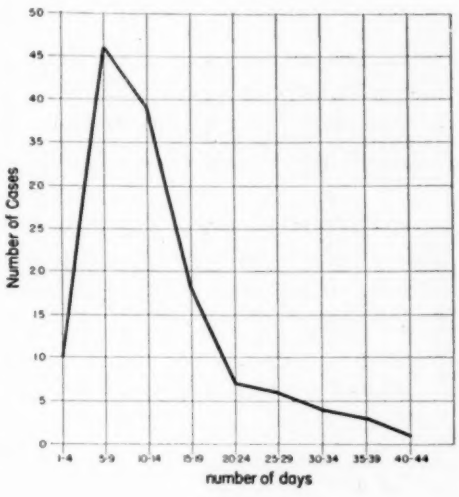

FIG. 2

FIG. 1.—Distribution by age.
FIG. 2.—Preoperative hospitalization in days.

Pain, frequently accompanied by dysmenorrhea, was the predominant symptom. The inflammatory symptoms usually over-shadowed those of uterine disease. Abnormal bleeding occurred 85 times, although there were only 14 submucous fibroids in the series. It is well known that this symptom frequently occurs in inflammatory disease, although its mechanism is not clearly understood. Seventy-nine of 135 cases gave a history of one or more previous attacks of pelvic inflammatory disease. Only 49 of 135 cases had had from one to four children. The high rate of infertility is expected with salpingitis.

Preoperative Hospitalization. The majority of cases required one to three weeks to fulfill Simpson's modified requisites.[3, 17] A sedimentation rate of 18 mm. in 30 minutes was attained preoperatively in all cases. Chemotherapy and in some instances antibiotic therapy were part of the preoperative treatment (Fig. 2).

Analysis of Operations.

Total hysterectomy	46
Supravaginal hysterectomy	85
Vaginal hysterectomy	4
Salpingo-oophorectomy (unilateral)	87
Oophorectomy (tube previously removed)	2
Appendectomy	15

Pathologic Condition of Salpinx at Operation.

Acute and subacute salpingitis (tubes thickened, acutely inflamed and tortuous)	34 cases
Pyosalpingitis (tubes swollen, retort-shaped, sausage-shaped, club-shaped, measuring 1.5 cm. or more in diameter)	44 cases
Chronic salpingitis (tubes thickened, densely adherent to peritoneum and adjacent structures)	57 cases

Postoperative Morbidity. One hundred thirty-three cases, or 85 per cent, were discharged on the tenth to the sixteenth day (Fig. 3).

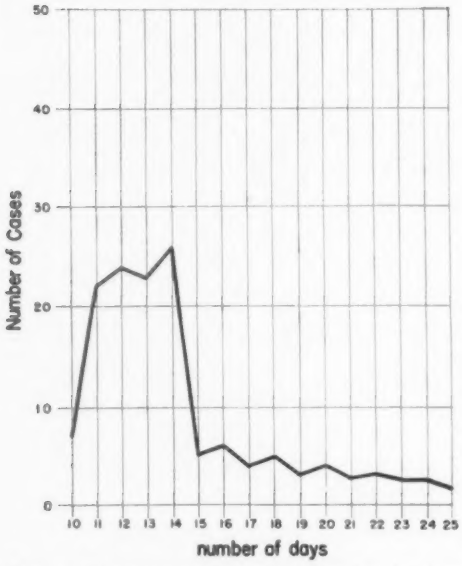

FIG. 3.—Postoperative hospitalization in days.

Postoperative Complications.

Wound infection	4
Cystitis	11
Pyelitis	1
Thrombo-phlebitis	4
Postoperative parametritis	1
Hemorrhage (vaginal cuff)	1

Postoperative Mortality. There was one death on the fourth postoperative day. At re-operation, mesenteric thrombosis was found and the patient died shortly thereafter.

Pathologic Condition of the Excised Ovaries. Unilateral salpingo-oophorectomy was performed 85 times for conditions tabulated below.

Cystic degeneration	71
Tubo-ovarian abscess	8
Brenner tumor	1
Dermoid tumor	1
Hydrosalpinx	4

In three cases, a normal ovary was excised, at the discretion of the operator, where trauma threatened the blood supply to the organ.

The primary indication was enlargement of the ovary due to cystic, suppurative, or neoplastic degeneration. In only four instances were adnexae removed because of gross abnormality of the tube (hydrosalpinx).

The high incidence of excised adnexae results from a radical attitude toward a cystic ovary, which may require re-operation. This principle, which uniformly interdicts "plastics of the ovary" in the presence of inflammatory disease,[5, 9, 10] is generally accepted.

Pathologic Condition of the Uterus. All these patients had fibromyomas of the uterus. In addition there were two cervical polypi, a fundal carcinoma and one endometrial polyp.

END RESULTS

Follow-up observation was obtained on 98 of 135 cases, over a period up to three and one-half years.

Anatomic Basis.

Cured		74%
Improved		24%
2–4 cm. adnexal masses	15	
Cervicitis	4	
Thrombophlebitis	1	
Failure		3%
Adnexal masses over 4 cm.	3	

Clinical.

Cured		85%
Improved		14%
Intermittent abdominal pain	4	
Dysuria	4	
Severe menopausal symptoms	4	
Leukorrhea	1	
Vaginal bleeding (polyp)	1	
Failure		1%

Economic.

Cured	87%
Improved	12%
Failure	1%

Re-operation. There is no record of re-operation on these patients, so far as we know, in this hospital or any other institution, for recurrence of infection in the retained tube.

SUMMARY

1. At Harlem Hospital one-third of patients who are admitted with myoma uteri have coincidental pelvic inflammatory disease of varying severity. Myomata uteri tend to occur at a younger age in Negro women so that at the time of operation ovarian conservation is frequently desirable.

2. Hysterectomy interrupts the epithelial continuity from the cervix to the tube and can be safely used for the treatment of adnexitis associated with myomata uteri. By leaving the tube and ovary in situ the vascular supply of the ovary is least jeopardized so that subsequent cystic degeneration is rare. Postoperative mortality, morbidity, and incidence of intestinal injury are lessened.

3. A total of 135 cases are reported with a clinical cure rate of 85 per cent; with a primary operative mortality of less than one per cent in this series.

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A CONTRIBUTION TO THE SURGICAL SIGNIFICANCE OF ABERRANT HEPATIC DUCTS*

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IN SUBDIAPHRAGMATIC VAGOTOMY, as in the mobilization of the cardia and subcardiaphragmatic part of the esophagus, access to the esophagus is made easier by severing the fibrous appendix and left triangular ligament of the liver. Our own experience confirms the data of the international literature—that, in so doing, we mostly sever relatively avascular tissue which, in the majority of cases, requires at most coagulation of a few small, slightly bleeding, vessels. By severing the above structures we gain a better survey of the cardiac part of the stomach and also facilitate the mobilization of the cardia and the abdominal part of the esophagus. This unpretentious procedure facilitates the removal of the lymphatics round the cardia at the lesser curvature, allows a better survey of the invasion of the carcinoma of the cardia into the diaphragm, and guarantees a more complete control of bleeding.

The severing of the fibrous appendix and of the left lateral ligament of the liver does not, in any way, endanger the postoperative course in the majority of cases. However, our observation, so far isolated, proves that this is not universally the case.

CASE REPORTS

Case 1.—A 51-year-old male patient, Joseph H., with extensive carcinoma of the stomach required total gastrectomy, which was performed on September 4, 1948, by Professor Rapant. A left oblique transrectal laparotomy determined the operability of the carcinoma. The laparotomy, after the costal arch was severed, was then extended to laparothoracotomy and the diaphragm was partly severed. At this stage we noted a whitish strip of 4 to 5 mm. in breadth, running subcapsularly along the convexity of the liver, which we assumed to end at the left lateral ligament of the fibrous appendix. This is an unusual observation to which we do not ascribe any importance, the nature of which we have no accurate idea, and which we consider to be without any practical consequence (Fig. 1). The fibrous appendix and left lateral ligament were transected with only slight bleeding, which was easily controlled by coagulation. We put towels over the mobilized left lobe of the liver and moved it to the right. Then the cardia was isolated and the severing of the diaphragm completed. The technically simple total gastrectomy was completed by an end-to-side anastomosis between the esophagus and jejunal loop, after Roux.

Before beginning the anastomosis between the esophagus and the jejunal loop, the towels were changed and we were surprised to notice bile stains. We ascribed this to an unobserved soiling by the duodenal or jejunal contents, which coulde have happened during the operation. After completion of the anastomosis and during the ensuing fixation of the jejunal loop to the margins of the opening in the mesocolon, we were greatly surprised by the intensive yellow coloring of the serosa of the mobilized jejunal loop, part of the mesocolon and posterior peritoneum. The reason for this staining was found in aberrant bile ducts in the fibrous appendix. These were closed by transfixing sutures.

* Submitted for publication April, 1949.

Case 2.—Soon after September, 1948, we made a similar discovery in another patient, 34 years old, F. V., suffering from peptic duodenal ulcer, in whom subdiaphragmatic vagotomy was carried out. In this case, a whitish strip of 3 to 4 mm. breadth appeared on the convex side of the left lobe of the liver about 6 mm. from the beginning of the fibrous appendix, into which it passed subcapsularly. Here it formed a small arch of 6 to 7 mm. in length and continued subcapsularly on the visceral side of the same lobe; there it gained a breadth of 2 to 3 mm. and a length of about 3 cm., and gradually disappeared in the parenchyma of the liver. A part of the fibrous appendix, together with the aberrant ducts, was resected for histological examination.

Microscopic examination of the tissue from the first patient disclosed subcapsular bile ducts in the whitish strips (Fig. 2). In the severed bile ducts aberrant hepatic vessels were observed (Fig. 3). In the resected parts from the second patient, islets of hepatic parenchyma were macroscopically visible, particularly after illumination and fixation in

FIG. 1.—Left lobe of the liver with broad subcapsular bile duct. Fibrous appendix tied.

formaldehyde. These were ill defined against their surroundings and without relation to the strips coming from the liver.

Microscopically, aberrant hepatic ducts of typical structure were observed in the subcapsular strips. The islets in the fibrous appendix were formed by an accumulation of hepatic cells, the nuclei of which were in the majority of cases stainable, but without formation of hepatic lobuli (Figs. 4 and 5). As compared with the first observation, the aberrant ducts were less developed; nevertheless, they were well defined. In addition, remnants of hepatic parenchyma were present in the form of not clearly limited islets in the fibrous appendix.

COMMENTS

E. H. Weber,[21] in 1843 defined aberrant ducts as subcapsular networks of bile ducts outside the hepatic parenchyma. Bile ducts of this kind were, however, already known to Ferrein[6] in 1753, who observed them in the left lateral ligament, and to Kiernan,[11] who described them in 1833 as a rudimentary liver. Aberrant ducts were systematically studied by Toldt, Zuckerkandl[20] (1875)

and Engel[5] in 1911. The name aberrant vessels, or ducts, is not quite adequate, and it appears to be useful to add "bile," in order to distinguish them from blood vessels which regularly accompany them, as well as from the aberrant

FIG. 2

FIG. 3

FIG. 2.—Part of a section through the large subcapsular bile duct above the left hepatic lobe. The epithelium is preserved only in the corners of the duct.

FIG. 3.—Aberrant vessels in the fibrous appendix of the liver.
Ducts A, B, C—pervious.
Duct D—impervious.
Duct E—closing.

structures in other organs. According to the frequency of their occurrence in different parts of the liver, they can be grouped as follows, according to Engel: most frequently they are in the connective tissue round the inferior vena cava

(round ligament), then on the left margin of the liver (left lateral ligament, fibrous appendix), in the fissure for the gall bladder, in the umbilical groove, the duodenal impression, the esophageal groove, on the base of Spiegel's lobe, in the transverse fissure, in the right lateral ligament and the hepatogastric ligament. The aberrant ducts form mutually anastomosing networks which are situated at different planes and are usually connected with the intrahepatic bile ducts. In the fibrous appendix the marginal branches are frequently connected in an arched manner (Fig. 6). The single branches, which end blindly, issue from this junction. During chronic biliary obstructions, both benign and malignant, the aberrant vessels can be considerably dilated (Counseller, 1928).[3] In

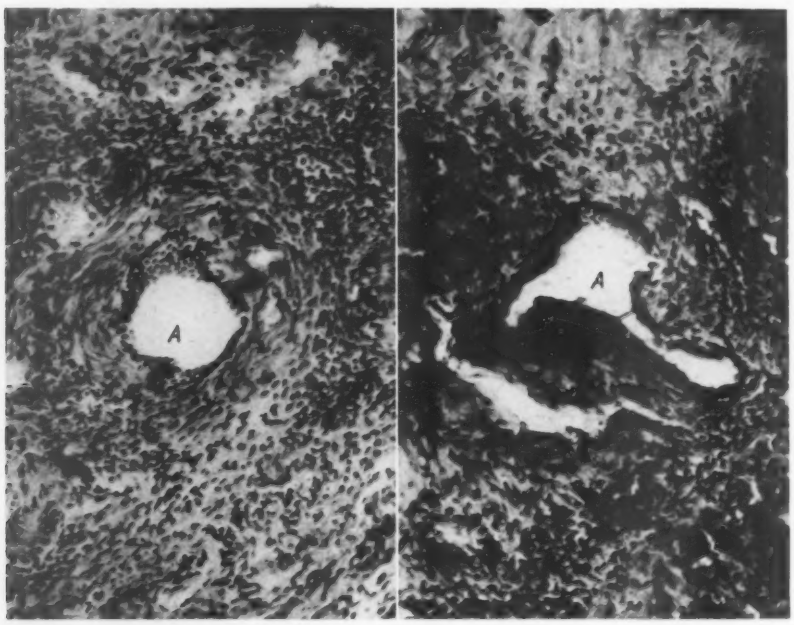

FIG. 4 FIG. 5

FIGS. 4 and 5.—(A) Aberrant duct of the liver. (B) Islet-shaped remnants of hepatic parenchyma.

addition to patent aberrant ducts, there may also occur impervious ones in the form of solid strips, or semipervious vessels. This depends on the degree of their development and their distance from the hepatic parenchyma proper. They are found regularly in the adult, but not always developed to the same degree. During old age they increase in number. In the child and fetus they are missing or rare. The case of Severi,[19] who found aberrant ducts in the periportal connective tissue inside the hepatic capsule of a 23-day-old girl, is not quite convincing. The date of their origin, however, is certainly to be placed in the fetal period. Aberrant ducts can be demonstrated macroscopically by gentle injection of the bile ducts from the hepatic duct.

The structure of aberrant ducts is identical with the structure of the intrahepatic bile ducts: a fibrous wall with a small number of elastic fibers and perhaps scattered muscle fibers. In well-developed patent ducts the fibrous tissue is clearly separated from its environment. With increasing distance from the hepatic parenchyma, the well-defined border is lost and gradually merges with adjacent parts. The lining is formed by one layer of cuboidal-columnar epithelium. Toldt and Zuckerkandl note that the epithelium decreases with the increase of distance from the hepatic parenchyma, until it finally disappears. It is important to bear in mind the experience of Lutkens,[14] in 1926, who found that the epithelium of the extrahepatic bile ducts is preserved only for about one hour after death, so that he abstained from examining the epithelium at

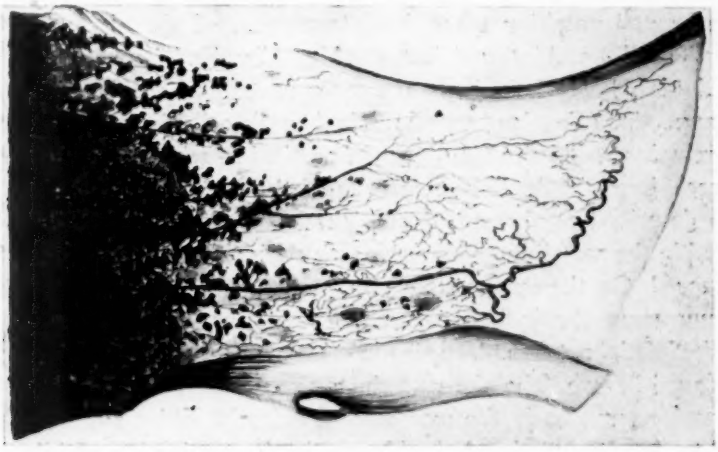

FIG. 6.—Fully developed network of aberrant ducts in the fibrous appendix (after Toldt-Zuckerkandl) accompanied by interstitial islets of hepatic tissue.

all. In our case, the epithelium is preserved in the majority of ducts with smaller lumina; in the biggest duct, which runs on the convex side of the left lobe, the epithelium is preserved only in the corners (Fig. 2). This can be explained by the damaging of the center of this duct by the hemostatic forceps during the ligature. The majority of authors describe bile duct glands in the walls of the ducts of the aberrant vessels. The glands can be atrophied, deformed or hypertrophied. In our case they occurred only in one part, which was not typical. This agrees with the observation that glands of the bile ducts of the parenchyma are present in the walls of major ducts only (Pfuhl,[16] Wolf[22]), and in the case of aberrant vessels the ducts are usually small.

The origin of aberrant ducts is explained in two ways: by a total reduction of the hepatic parenchyma in places where it occurred initially, with preservation of the bile ducts, or by cessation of the development of the bile ducts. Moschzowitz[15] is alone in his opinion that aberrant ducts are of teratogenic nature, the primitive endodermal tubuli not having formed hepatic cells as they

should. The progress of the reduction of the hepatic parenchyma was studied by Toldt and Zuckerkandl[20] on the left lobe of the liver. They found that, from the hepatic mass, at first strips of tissue remain, then gradually islets of normal tissue, later islets of tissue of indistinct structure, and finally only bile ducts with blood vessels. This process exactly corresponds to the developmental diminution of the left hepatic lobe. As is known, the lobes of the liver are initially symmetrical, and the left may even be bigger (Schaffer[17]) because of better arterial blood supply resulting from the opening of the umbilical vein, carrying arterial blood, into the left branch of the portal vein. Only secondarily the reduction of the parenchyma takes place. The pressure of the adjacently growing organs—mainly the stomach and the replaced physiologic umbilical hernia—is generally given as a reason for the reduction, as well as the deteriorated nutrition after the interruption of the placental circulation (Langer-Toldt[12]) and internal factors (Max Clara[2]). The result is the diminution of the left lobe of the liver, the outer part of which finally becomes the fibrous appendix (Frankenberger[7]). The hepatic cells disappear, but the blood vessels remain; so do the bile ducts in particular, which may, in certain circumstances, hypertrophy. The remnants of this hepatic tissue, the bile ducts, are then described as aberrant ducts. These, together with the blood vessels, are placed in the remaining connective tissue which, in the majority of cases, is not increased. On the surface they are surrounded by a fibrous capsule containing numerous elastic fibers. A process of reduction, similar to that occurring in the left lobe, takes place also in other parts of predilection in the liver, as mentioned before. The aberrant ducts are not a peculiarly human characteristic and occur also in the majority of animals. Elder authors (Weber[21]) ascribed to them a functional significance in the production of bile, but from the slight extent of these ducts, it may be assumed that their functional significance is negligible, if it exists at all.

SUMMARY

From a practical point of view, only the significance of aberrant bile ducts in the gallbladder fissure was known—the so-called ducts of Luschka which, if opened during cholecystectomy, are the source of biliary drainage during the first postoperative days. Pathologico-anatomically, aberrant ducts used to be named in connection with cases of cysts (Hlava,[9] Aschoff[1]), cystadenoma (Domagh[4]) and cavernoma (Ludwig in Henke-Lubarsch[13]).

We have considered it useful and advantageous to draw attention to the existence of aberrant bile ducts in the fibrous appendix, the unintentional severing of which might cause grave postoperative complications, particularly in cases where not only the peritoneum (in subdiaphragmatic vagotomy), but also the pleura (in phrenothoracolaparotomy) is exposed to irritation by bile. We are aware of the relative rarity of this developmental anomaly, but it is not out of the question that, with the increasing number of operations upon the vagus nerve, the cardia and lower part of the esophagus, our observation may gain considerable practical significance.

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The microphotographs were made in the Anatomical Institute of Masaryk University, Brno, by the assistant, Mr. Dolezel, M.D., to whom we express our gratitude.

THROMBOPHLEBITIS MIGRANS*

CASE REPORT WITH AUTOPSY AND REVIEW OF LITERATURE

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THROMBOPHLEBITIS MIGRANS is a disease in which phlebitis usually appears in small segments of superficial veins, also in deep and visceral veins, and is characterized by multiple recurrences widely varied in time and location. This condition must be differentiated from the so-called "creeping thrombophlebitis" which primarily involves one or more veins by gradual extension. Thrombophlebitis migrans has long been established as a disease entity. Jadioux[1] in 1845, Frèmy[2] in 1864 and Paget[3] in 1866 reported cases which belong to this category. Briggs[4] in 1905, was the first to use the term "idiopathic recurrent thrombophlebitis" and it appears that Hedblom[5] in 1916 was the first to use the term "thrombophlebitis migrans."

In a review of the available literature,[1-27] more than 100 cases of thrombophlebitis migrans have been reported; however, only 12 cases meeting these criteria have come to autopsy.[6-13] It appears that one case reported by Stern[8] and one case reported by Gerber and Mendlowitz[13] do not fit into this category. Thrombophlebitis migrans is probably more common than is generally indicated in the literature. All who have had considerable experience with thrombophlebitis can readily recall cases which differed from the usual type, in that, despite adequate treatment and apparently good response, recurrences were frequent and widespread. It is important that a more careful evaluation of the history and physical findings be made to avoid errors in management of thrombophlebitis migrans. A case report with autopsy is presented to emphasize further the possible pitfalls in treatment of this condition.

Case Report.—J. B., a 25-year-old white male, was admitted to the hospital on September 8, 1948, complaining of cramplike abdominal pain and vomiting of 3 days' duration.

Past history indicated the patient developed swelling in the right elbow region in the Fall of 1939. In the Spring of 1941 he developed pain, swelling and tenderness in the left leg, associated with chills and fever. He stated that two weeks prior to this episode he experienced pleurisy on the right side. Residual swelling of the left leg continued. He entered the Naval Service in December, 1942, but was discharged the next month because of swelling and stasis ulcer of the left leg. Later that year the superficial veins of the left leg were ligated in a civilian hospital. He was admitted to this hospital on

* Sponsored by the VA and published with the approval of the Chief Medical Director. The statements and conclusions published by the authors are a result of their own study and do not necessarily reflect the opinion or policy of the Veterans Administration.
Submitted for publication August, 1949.

March 12, 1943, for acute thrombophlebitis of the right leg and stasis ulcer of the left leg, and received symptomatic treatment. There were admissions on January 2, 1944, December 26, 1944, and June 8, 1945, for varying degrees of thrombophlebitic activity in both legs and stasis ulcers of both legs; only symptomatic treatment was rendered in each instance. The next admission was in August, 1946, for recurrent thrombophlebitic activity in both legs, when a trans-abdominal vena cava ligation was attempted but found to be technically not feasible. He responded to anticoagulant therapy. On November 19, 1946, he was again admitted for recurrence of pain and swelling in both legs, and on November 27, 1946, a vena cava ligation by retroperitoneal route was accomplished. The

FIG. 1 FIG. 2

FIG. 1.—Infrared photograph. Thrombosis and dilatation superficial abdominal veins.

FIG. 2.—Stasis pigmentation, superficial ulceration and scarring.

next admission was March 20, 1947, for acute thrombophlebitis of superficial veins of the left lower abdomen (Fig. 1). Thrombophlebitis in the legs continued, and a left lumbar sympathectomy was performed on June 11, 1947, followed by a course of anticoagulant therapy. On March 3, 1948, he was again admitted for acute thrombophlebitis of superficial abdominal veins, responding satisfactorily to Dicumarol therapy. He was re-admitted 4 months later with partial intestinal obstruction and acute thrombophlebitis of the superficial abdominal veins. Preliminary intestinal decompression and separation of abdominal adhesions was done on August 11, 1948. Dicumarol therapy was employed postoperatively. Discoid atelectasis in the base of the left lung was noted on a post-operative roentgen ray film on August 20, 1948.

Physical examination on admission revealed a well-developed, obese, white young male, who appeared to be dehydrated and acutely ill, but was alert, oriented and co-operative. The abdomen was tender in the peri-umbilical region and there was post-operative weakness of the anterior abdominal wall but no hernia. The abdomen was not

distended. There were thrombosed superficial veins in the upper extremities. The legs showed marked stasis pigmentation and superficial scarring (Fig. 2). The examination otherwise was negative.

Laboratory Examination. September 10, 1948: serology negative, W.B.C. 10,700; hemoglobin 14 Gm.; urine negative. September 17, 1948: urine negative; bleeding time one minute; coagulation time 3 minutes.

Clinical Course. On admission 3000 cc. of parenteral fluids were administered daily, but no oral intake was permitted. There was intermittent gastric aspiration and intermittent emesis, but abdominal distention developed, varying between minimal and moderate, and continued until September 20, 1948, when an abdominal exploration was performed and multiple loops of small intestine were released from a moderate postoperative adhesive process. One small rent was accidentally made in a loop of small intestine, but

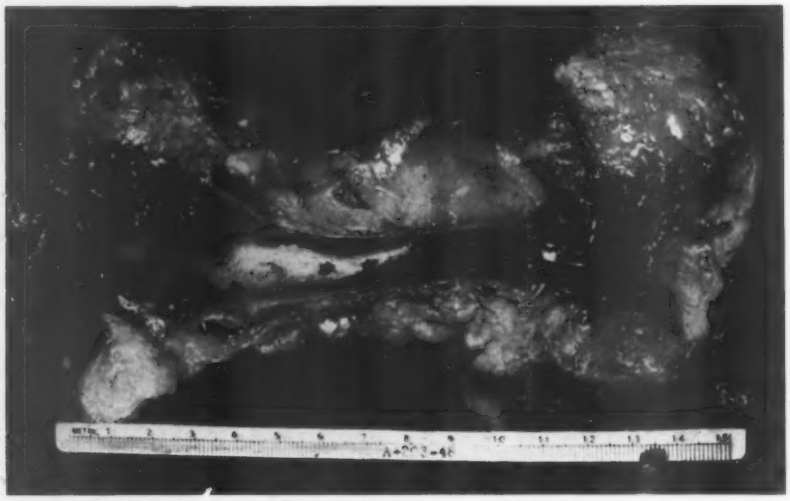

FIG. 3.—Gross specimen: Thrombosis of splenic vein.

was closed without difficulty. During and immediately after operation, 1000 cc. of blood was administered. The patient's immediate postoperative condition was good and progress satisfactory on routine postoperative treatment. On the morning of September 23, 1948, a liquid diet was taken and well tolerated. On the afternoon of the same day he experienced severe pain in the left lower quadrant of the abdomen which was continuous but became worse in a cyclic manner. The abdomen was locally tender and no peristalsis could be heard. The patient was operated upon the following day and, in addition to the chronic adhesive peritonitis described above, the intestinal coils were found to be covered with serofibrinous exudate in several areas. There was no evidence of perforation of the intestine and the serofibrinous peritonitis could not be accounted for. The patient went into deep shock shortly after operation, and in spite of 950 cc. of blood and other parenteral fluids, he failed rapidly and died at 8:30 P.M., September 25, 1948. Autopsy was performed by Dr. Miles B. Smith.

Autopsy. The body was that of a well-developed, well-nourished, young, white male. There were noted two recent and four healed surgical scars over the lateral and anterior abdominal wall, and marked pigmentation and scarring of both legs. Examination of the thoracic cavity revealed a few thin, fibrous adhesions between visceral and parietal pleurae bilaterally. The lungs were markedly congested bilaterally and there was noted

hemorrhagic infarction in the inferior portion of the left lower lobe. The heart and aorta were grossly normal. The abdomen contained 200 cc. of yellowish brown, cloudy fluid. The abdominal viscerae were covered with an adherent, yellowish tan, fibrinous membrane extending from the right lower quadrant on the anterior surface of the small bowel to the left upper quadrant. The serosa was red and dull throughout. The liver and kidneys showed parenchymatous degeneration. The spleen weighed 570 Gm. and was partially covered with fibrinous yellowish tan shreds. There was infarction of the entire inferior pole and scattered small areas of infarction throughout the remainder of the spleen. Branches of the splenic vein contained recent thrombi (Fig. 3). The proximal 40 cm. of the jejunum was dilated to a diameter of 8 to 10 cm. Beginning approximately 35 cm. distal to the ligament of Treitz and extending for a distance of 25 cm., the bowel wall was of a purplish red color and extremely friable. The hemorrhagic discoloration extended into the adjacent mesentery for a distance of 10 cm. Dissection of the mesenteric veins in this area showed complete occlusion by recent thrombi which extended into the main trunk of the superior mesenteric vein (Fig. 4). The lumen of the portal vein was also partially occluded by a recent thrombus. In the proximal ileum there was seen a 10 cm. segment of bowel which was of a purplish red color and markedly friable. Dissection of the adjacent mesenteric veins revealed recent thrombosis extending into the superior mesenteric vein. The vena cava was unchanged to a point 8 cm. below the right renal vein, where sudden narrowing and complete obliteration was found. The vena cava and iliac veins were fibrous cords below this level. The adrenal glands, urinary bladder, prostate gland, testes, thyroid gland, pancreas, stomach, duodenum and colon were essentially normal.

FIG. 4.—Gross specimen: Thrombosis of mesenteric veins

Pertinent anatomical diagnoses were: (1) marked pigmentation and superficial scarring of both lower extremities, (2) marked bilateral pulmonary congestion and hemorrhagic infarction of inferior portion of the left lower lobe, (3) acute peritonitis, (4) infarction of inferior pole of spleen, (5) multiple thromboses of mesenteric, splenic and portal veins, (6) infarction of jejunum and ileum, and (7) fibrous obliteration of lower vena cava and iliac veins.

The cause of death was generalized peritonitis, resulting from thrombosis of the mesenteric veins, due to thrombophlebitis migrans.

Microscopic Examination. The heart showed minimal fibrous infiltration and minimal thickening of the intimal layer of the coronary arteries. The aorta also showed minimal focal areas of intimal thickening. Sections of the lung revealed marked congestion, infarction and scattered areas of bronchopneumonia. The liver parenchyma showed a moderate degree of cloudy swelling. The splenic capsule was covered with an acute inflammatory fibrinous substance, while the splenic substance showed areas of infarction. The tubules of the kidney showed parenchymatous degeneration and marked congestion

of the vessels. The urinary bladder was normal with the exception of marked congestion of small vessels. The prostate, pancreas, thyroid and testes were essentially without change. Marked edema and beginning necrosis of the mucosa and muscularis of the small intestine were noted. Various sections from the thrombosed mesenteric veins show very recent and partially organized thrombi completely filling the lumina of the vessels (Fig. 5).

DISCUSSION

FIG. 5.—Photomicrograph: Thrombosis of mesenteric vein.

The etiology of thrombophlebitis migrans remains obscure. Gout, arthritis, phlebosclerosis, unknown toxins, sensitivity to tobacco, various bacteria and many other agents have been named as possible causes. It is a disease of the young and middle aged. Cases are reported from six to 57 years of age; the average being slightly less than 40. It appears to be about four times as common in males as in females.

The phlebitis of Buerger's disease may be migratory in nature in about 40 per cent of cases, and must be carefully ruled out in the differential diagnosis. Buerger's disease, however, involves both arteries and veins, is primarily inflammatory in nature, and is usually associated with a marked disturbance in the vasomotor mechanism. From time to time it has been suggested that thrombophlebitis migrans is a type of Buerger's disease involving only veins on the basis that some of the thrombi resembled those of the latter. There is, however, no real evidence that the two conditions are etiologically related.

Manson-Bahr and Charters[14] have recently reported a virus similar to that of infectious hepatitis as being responsible for recurrent thrombophlebitis. It is apparent, however, that a different disease was being considered. The cases reported by these authors differed in that the disease appeared in epidemic proportions. There was sometimes an associated stiff neck, the leukocyte count was usually below 8000 or 10,000 with a relative lymphocytosis, and an entire vein was frequently involved. These are not the findings of thromboplebitis migrans.

Barker,[15] in 11 of his cases, removed a segment of the affected vein. The cultures were uniformly sterile. The thrombus histologically was highly cellular, and the inflammatory reaction in the wall of the vein and adventitia was pronounced. These histological findings, however, are not consistent and frequently may be impossible to differentiate from any other non-bacterial thrombophlebitis.

The superficial veins of the extremities and to a lesser degree abdomen and thorax are most frequently involved. The segment of vein involved in the thrombophlebitic process is usually small, gives rise to tenderness and redness and subsides in a matter of days or weeks. Weeks, months, or years thereafter, another vein, most commonly remote from the first, becomes involved. Deep veins of the extremities, neck and eventually those of the abdominal viscera, lungs, heart, and even the brain may become involved. Usually most of the pulmonary lesions are actually small emboli from other foci. Fever and leukocytosis commonly accompanies each new attack. Involvement of visceral veins is the most serious complication. Mesenteric veins are more frequently involved than any of the other visceral veins.[1-27] Five[6, 8, 10, 13] of the 13 reported cases coming to autopsy died of mesenteric thrombosis.

There is no specific therapeutic agent of curative value for thrombophlebitis migrans. The use of anticoagulants appears to be the only rational approach to therapy. Heparin and Dicumarol are highly beneficial in limiting the duration and extent of each recurrence. No long range benefit is expected; however, if anticoagulant treatment is initiated early, morbidity is markedly decreased and many of the more serious complications prevented. Ligation is not ordinarily recommended because emboli, when they occur, are small and the procedure itself can hardly be expected to limit a process which is characterized by recurrences in widely disseminated areas. However, it may be useful in treating the postphlebitic syndrome of the lower extremities.

COMMENT

The case presented follows, in most respects, the typical history of thrombophlebitis migrans. The recurrences were unpredictable and even symptomatic treatment alone, in several instances, appeared to be adequate. The disease, except in its late stages, is quite benign; however, it results in much disability and anxiety.

The patient was initially considered an ordinary case of thrombophlebitis and repeatedly treated as such by ligation and anticoagulants. The transabdominal approach to the vena cava on the first attempt may have contributed to the intestinal adhesions and the subsequent intestinal obstruction. Vein ligation can only limit thrombophlebitis migrans locally and should be employed reluctantly. Vein interruption, however, may be considered either when a large vessel is involved, and there is real danger of a large embolus, or for therapy of stasis ulcer. In this case, anticoagulant therapy was used repeatedly for the recurrences and the vena cava ligation was a desperate effort to stop the continuing progress of the disease. Some benefit apparently resulted from these measures, because from March, 1947, to March, 1948, he was gainfully employed. The ligation also helped the stasis ulcers on both legs.

In this case, autopsy did not reveal a focus within the general circulation from which a thrombus might have separated to cause pulmonary infarction. It is reasonable to assume, therefore, that thrombosis within the pulmonary vessels was primary.

CONCLUSIONS

1. A case of thrombophlebitis migrans with fatal outcome and autopsy is reported.

2. The etiology remains obscure and at least for the present is classified as a primary idiopathic thrombophlebitis.

3. Histologically, the thrombus is not characteristic, although it may be highly cellular and the inflammatory reaction in the wall of the vein and adventitia may be pronounced.

4. Small segments of peripheral superficial veins are most commonly involved, but no vein is immune, and the disease is characterized by recurrences widely spaced in location and time.

5. Ligation is ineffective in confining a disseminated disease; however, it can be considered where there is threat of large emboli or in treating postphlebitic ulcers.

6. Anticoagulant therapy, although without long range benefit, is usually effective in limiting the duration and extent of each recurrence.

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CALCIFIED INTRACEREBRAL HEMATOMA*

CASE REPORT AND REVIEW OF THE LITERATURE

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IN A LARGE SERIES of surgically treated cerebral vascular accidents,[16] the occurrence of a calcified intracerebral hematoma prompted an investigation of the literature on the subject of intracerebral calcifications. Grantham and Smolik,[12] in reporting their case in 1942, stated that only one other such case appeared in the medical literature up to that time.

Case Report.—E. F. B., A 23-year-old, white male, was admitted to the Merced, California, Hospital with complaints of weakness and numbness of the left side of the body and impairment of speech.

Past History. He was well until four days prior to his admission, when he had a sudden lancinating pain over the right side of his head. Later in the day he noticed that he was having trouble holding objects in his left hand. Within three hours the weakness had spread to involve the left trunk and lower extremity. Within five hours he had marked impairment of speech, severe headache and nausea. He was hospitalized and roentgen rays of the head revealed intracerebral calcification and an enostosis of the right parietal skull (Fig. 1). A diagnosis of meningioma was considered in view of these findings and he was transferred to this hospital for operation.

Examination. This showed a lethargic young, white male with an apparent left hemiparesis. Blood pressure was 120/64. The pupils were equal in size and responded to light. There was no papilledema on fundoscopic examination and the visual fields were normal. An ovoid tumor mass about three cm. in diameter was seen in the right parietal scalp over the previously noted enostosis of the skull. There was a central type of left facial weakness present. The reflexes were increased in the left extremities but pathologic toe and finger signs were absent. There was a complete astereognosis of the left hand. He exhibited an incomplete motor aphasia and alexia without apperceptive difficulty.

The spinal fluid was clear and the pressure was 130 mm. of water. A right common carotid arteriogram was done. The arterial phase (Fig. 2) revealed no significant displacement of the vessels. The venogram (Fig. 3) demonstrated abnormally large vessels that were displaced by a mass containing the calcium seen in the plain film of the head.

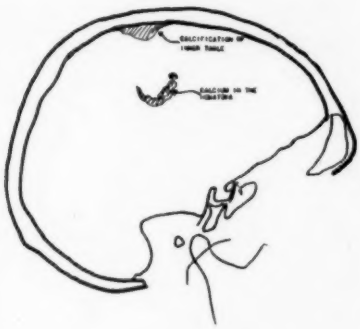
Operation. He was prepared for craniotomy. The ventriculogram (Figs. 5 and 6) revealed displacement of the ventricular system consistent with a high right parietal mass. A free bone flap was made in the right parietal area. On opening the dura the abnormally large venous channels were seen lying on the surface of the cortex. The mass was found at a depth of three cm. beneath the surface of the cortex. It contained old organized clot, calcium, and some recent semi-solid clot. After evacuation of the hematoma a smooth-walled cavity without bleeding points remained.

The patient's postoperative course was uncomplicated. He recovered from his hemiparesis and aphasia. A two-year follow-up has been unremarkable.

* Sponsored by the Veterans Administration and published with the approval of the Chief Medical Director. The statements and conclusions published by the Authors are a result of their own study and do not necessarily reflect the opinions or policies of the Veterans Administrations. Submitted for publication August, 1949.

FIG. 1A

FIG. 1B



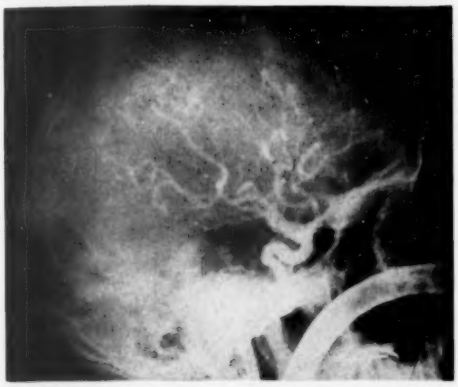


FIG. 2A

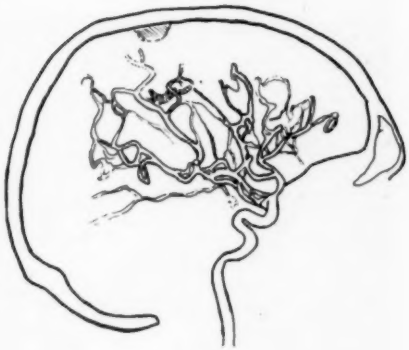


FIG. 2B

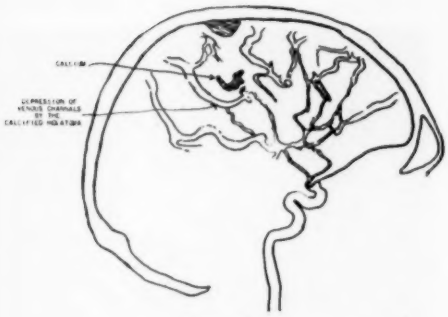


FIG. 3B

FIG. 3A

FIG. 1.—Roentgen ray and tracing of skull showing enostosis and calcification in hematoma.
FIG. 2.—Arterial phase of angiogram with no displacement of arteries.
FIG. 3.—Venous phase with displacement of venous channels by calcified mass.

FIG. 4A

FIG. 4B

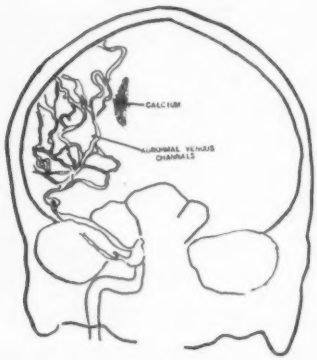


FIG. 5A

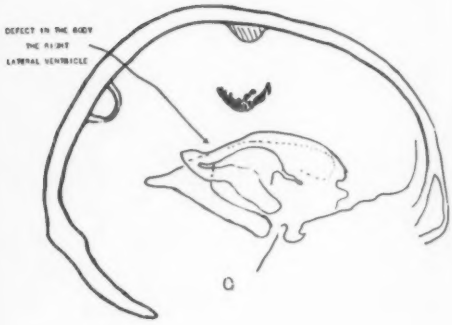


FIG. 6A

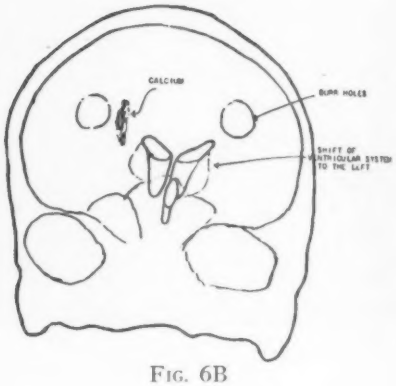


FIG. 6B

FIG. 4.—A-P angiogram of the mass.
FIG. 5.—Lateral view ventriculogram showing displacement of ventricle.
FIG. 6.—A-P ventriculogram of foregoing.

DISCUSSION

Four cases of operative removal of calcified intracerebral hematoma were found in the literature (Table I).

Buckley[5] reports a calcified hematoma found at autopsy in the right parietal lobe of a patient who had epilepsy for 23 years. Levin[15] in his report describes a second case with a large calcified mass in the left tempero-parietal area that he believed to be a calcified hematoma. Oberndorfer[18] reports operating on a calcified vascular lesion with "extensive calcification of the brain substance." O'Sullivan[20] describes two cases of calcified hemorrhage of the brain stem and basal ganglia. Penfield and Geyelin[21] removed the right occipital lobe in a patient with a large calcified mass, presumably of vascular origin.

TABLE I

Surgeon	Date	Age Sex Race	Symptoms	Location of the Hematoma	Follow-up	Histology
Miller[17]	1922	60 F W	Epilepsy 26 years Left headache	Left parietal lobe	No epilepsy since surgery	Calcium-oxalate Old blood elements
Petitpierre[22]	1926	21 M W	Epilepsy	Right parietal lobe	Not given	Calcium Old clot
Levin[15]	1927	21 M Indian	Epilepsy 16 years	Left tempero-parietal	No epilepsy since surgery	
Grantham & Smolik[12]	1939	42 M C	Epilepsy 33 years	Right occipital lobe	Not given	Necrotic tissue, calcium

Camp[6] in a review of calcified vascular lesions of the brain groups them into (1) aneurysms, (2) angiomatous malformations and (3) hematomas. It would appear that calcification in aneurysms is the most frequent of these lesions except for the type occurring around the great cerebral vein as described by Oscherwitz[19] and Alpers.[1]

The occurrence of intra-cranial calcifications in patients exhibiting facial nevi has been discussed by Bentzen,[2] Eaves,[10] Cushing and Bailey[8] and by others. In our case the presence of the lipoma of the scalp, with its underlying enostosis, intracerebral calcification and vascular abnormalities (Figs. 1 and 3), again emphasizes the association of lipoma and other abnormalities of the ectodermal derivatives with vascular malformations of the central nervous system. Berenbruch,[3] in 1895, was one of the earliest observers to comment on this. This association has since been the subject of intensive investigation until the term "phacomatoses" is now used to mean a wide-spread disease of congenital origin involving the ectodermal and mesodermal derivatives. Ehni and Love[11] and others[7] have recently discussed this syndrome.

Hamby,[13] Jander,[14] Schiele,[23] and Zollinger and Gross[24] discuss the fate of the intracerebral hemorrhage and the process of calcium formation. It has

been pointed out by Browder and Turney[4] that intracerebral extravasations of blood coagulate in a few hours; they found clotted blood in patients dying a few hours after injury. In those surviving for 15 hours the clot had become liquid and suitable for aspiration.

The prediliction of calcifying lesions for the parietal and occipital lobes has been noted. Bentzen[2] noted in a review of 75 cases of calcification of the pia that 46 per cent of them occurred in the occipital lobes.

SUMMARY

1. A case of calcified intracerebral hematoma of the right parietal lobe in a young man with surgical treatment and recovery is discussed.

2. The four previously reported cases are reviewed.

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TRI-LOCULAR GASTRIC DIVERTICULUM

TREATED BY SURGICAL EXTIRPATION THROUGH THORACO-ABDOMINAL INCISION*

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HISTORY

Gastric diverticula were first described in 1661 by Moebius and in 1774 by Roax.[1] Helmont,[2] in 1804, was another early writer who described this unusual condition. True gastric diverticula have been reported in the stomachs of hogs (by Keith[3]) and in one type of primates (by Boppe[4]). The occurrence of the condition in these animals is quite common as compared to its rarity in the human species.

INCIDENCE

Bochus[6] and Moses[1] in different reports, both in 1946, stated that there were only slightly more than 150 reported cases at that time. In some of these, the diagnosis was not definitely established.

Rivers, Stevens and Kirklin[7] in 3662 routine autopsies found four gastric diverticula. In the roentgen examination of the stomach in 782 patients, Shiflett recorded an incidence of 0.65 per cent.

CLASSIFICATION

Gastric diverticula have been classified by Schmidt and Walters[8] as follows: (1) True (congenital) diverticula, in which all layers of the stomach are present, and which type is due to malformation or interrupted development during the fetal period. (2) False (acquired) diverticula, which are secondary to some other type of gastric pathologic condition or mechanical physiologic phenomenon. The false diverticula are further subdivided into the following group: (a) pulsation type, which may be secondary to difficult labor, pyloric obstruction, severe vomiting, coughing, constipation, foreign bodies, etc., producing increased intraluminal pressure or which may result from the eroding effect of gastric ulcers or carcinoma; (b) the traction type, (due to perigastric adhesions resulting from inflammatory lesions of the spleen, gallbladder, pancreas, liver, or peritoneum).

In this communication, we are primarily interested in the true or congenital type of gastric diverticulum.

EMBRYOLOGY AND ANATOMY

Approximately 65 per cent of all gastric diverticula occur close to the lesser curvature on the posterior wall of the cardiac end of the stomach. An

* Submitted for publication, August, 1949.

even higher percentage of true diverticula occur in that location. According to Reich,[9] this is due to the fact that at this site the longitudinal muscle divides into two muscular fasciculi and therefore the mucosa is only surrounded by circular muscle fibers. Reich has reported that the diverticula have been found in the human embryo, suggesting that its presence in adults is due frequently to a persistence of a fetal diverticulum.

The diverticula are usually pear-shaped and small with narrow orifices, although wide-neck sacs have been reported. A true gastric diverticulum rarely exceeds two cm. in diameter. Retention of gastric contents in the sac is more apt to occur in those with a small orifice. True gastric diverticula are usually unilocular. However, cases of multilocular gastric diverticula have been reported. The case herein reported represents a rare type of tri-locular diverticulum.

CLINICAL PICTURE

True gastric diverticula may occur at any age. They are most common between the ages of 30 and 50. The sex incidence shows a predominance of females in a ratio of approximately two to one.

A large percentage of gastric diverticula are asymptomatic. This is demonstrated by the fact that many diverticula are found on roentgen ray examination of the stomach when it is definitely known that these are not producing symptoms. Furthermore, numerous incidents of gastric diverticula are recorded in autopsy statistics. The clinical records in these cases often reveal no evidence of abdominal discomfort referable to the diverticula. When a gastric diverticulum does produce symptoms, the clinical picture is not definitely characteristic. The symptoms are produced by the diverticulum filling up with food and gastric juices. It is then unable to evacuate itself because of the usual small size of the orifice and the kinking of the neck which occurs when it is filled.

The most common symptom is epigastric pain and fullness, which most often occur shortly after meals. The pain is frequently deep seated and may radiate into the lower retrosternal region. In large size diverticula, dysphagia may be present. True gastric diverticula in the region of the cardia are a known cause of cardiospasm.

Nausea and vomiting are not uncommon symptoms. Massive hemorrhage, due to secondary ulceration, has been recorded by Sutherland,[10] Brown and Priestley,[11] Hillemand,[12] and others.

Belching, epigastric tenderness and abdominal distension are sometimes present. In rare instances, the pain may be relieved by the taking of food. The literal derivation of diverticulum is "a wayside house of ill fame" and a gastric diverticulum lives up to this reputation in that the retention of food usually encourages inflammation of the mucosa with subsequent pain and discomfort. This inflammation may progress, as previously mentioned, to ulceration, peridiverticulitis, and hemorrhage.

It is seen from the above discussion that the clinical picture is by no means

typical. The diagnosis of gastric diverticulum can be made only by roentgen studies of the barium-filled stomach. Even when this examination is made, if the upper portions of the stomach are not carefully studied with the patient in different positions and again after the barium has been evacuated from the stomach proper, small diverticula may be overlooked.

Characteristically, the typical congenital gastric diverticulum usually manifests itself as a small, sac-like protusion from the posterior aspect of the cardiac end of the stomach close to the lesser curvature. It is usually unilocular, but as previously mentioned, may be multilocular. The larger diverticula frequently show a tendency not to empty themselves of barium as rapidly as does the remaining part of the stomach.

Even if a gastric diverticulum is definitely discovered at roentgen examination, the remaining portion of the stomach and duodenum, as well as the biliary system, must be carefully examined. The mere presence of a gastric diverticulum on roentgen ray examination does not necessarily mean that it is the cause of the patient's symptoms. As previously stated, a large percentage of gastric diverticula do not produce symptoms.

Gastroscopic examination aids in the study of these cases—particularly in differentiating between a true diverticulum or one secondary to some other type of gastric pathologic condition. The orifice of the true diverticulum has the appearance of a circular hole—the margins of which are well rounded and sharply defined. The surrounding mucosa is usually normal and there is no sign of infiltration. On the other hand, a penetrating gastric ulcer usually has a base which is covered with a gray or white exudate, or is more rarely covered with blood. The surrounding mucous membrane usually shows an inflammatory reaction. A penetrating carcinoma usually shows signs of ulceration at the base of the tract and the surrounding margins are irregular and infiltrated.

If there is any question whatever as to the possibility of a gastric diverticulum being secondary to a gastric ulcer, whether it be benign or malignant, the patient should be subjected to surgical exploration regardless of the relative mildness of the symptoms.

Because of the excellent blood supply to the cardiac end of the stomach, the mobility and activity of the stomach as a whole, and its relative freedom from bacteria, gastric diverticula do not present the numerous complications usually associated with diverticula of the colon. Serious complications of gastric diverticula are uncommon. Hemorrhage is the most frequent complication and occasionally may be severe. Moses[1] and others have recorded instances in which true diverticula of the stomach have perforated. This complication, however, is extremely uncommon.

TREATMENT

The majority of cases of symptomatic gastric diverticula can be treated medically. Those cases, in which no symptoms are present, need no specific treatment.

In the cases which produce only mild symptoms and in which there has been no evidence of serious hemorrhage, impending perforations, or associated gastric ulcer, conservative treatment should be tried. A bland diet with antacids and antispasmodics will often relieve the symptoms. Postural drainage has been suggested by Hurst and Briggs.[13] By fluoroscopic observation, it may be possible to find the position which favors the emptying of the pouch.

Surgical extirpation of the diverticulum is indicated if the symptoms are severe and do not respond to the above mentioned medical measures. Furthermore, the occurrence of massive hemorrhage and the uncertainty of the presence of other gastric abnormalities (particularly gastric ulceration, either benign or malignant) are definite indications for surgery.

The actual manner of surgical approach to a gastric diverticulum, which is usually situated in a very unavailable location, is one that has produced much discussion.

Lahey,[15] Walters[14] and other capable abdominal surgeons have reported successful removal of the diverticula by the transabdominal route. However, Lahey[15] has stressed the inaccessibility of these lesions, when they are situated in the usual position close to the cardia on the posterior wall near the lesser curvature, and has emphasized the many technical difficulties. He recommends that surgery be performed only as a last resort.

In our opinion, the most direct approach to this portion of the stomach should be either through a transthoracic and transdiaphragmatic incision or by means of a combined thoraco-abdominal incision, as recommended by Humphreys,[16] Kremen,[17] and others for high gastric lesions.

In the case reported herein, a thoraco-abdominal incision was used similar to that suggested by Humphreys.[16] The experience, in this single case, was gratifying and it is our opinion that such an approach has definite advantages. The abdominal, thoracic, and diaphragmatic components of the incision need not be as extensive as those used for performing radical gastrectomies or esophagogastrectomies through the same approach. The mobilization of the greater curvature of the stomach and the rotation of the stomach in order to expose the diverticulum is easily attained. With the recent advances that have been made in thoracic surgery and the impunity with which surgeons now open the thoracic cavity, there is certainly at present little or no justifiable argument in favor of the abdominal approach.

Furthermore, the surgeon who has been trained primarily in abdominal surgery will, as Kremen[17] has emphasized, find the abdomino-thoracic incision advantageous. He is thereby placed on more familiar ground and the operation is performed from a customary stance and position at the operating table.

CASE REPORT

Miss R. B., white female, age 21, was admitted to Touro Infirmary on February 20, 1948. For 18 months she had suffered from upper abdominal symptoms, at first mild, but which became progressively more severe. These symptoms consisted of nausea, upper

abdominal cramps, and epigastric fullness. All were directly related to the taking of food and occurred immediately after eating. They were not related to the taking of any particular type of food.

At the time of admission to the Hospital, the patient was no longer able to eat a full meal and was existing on numerous small feedings, which produced less severe symptoms. It had been known for a period of six months that the patient had a gastric diverticulum. During this time she had received the usual medical treatment of a bland diet, antispasmodics, alkalis, etc.

The patient was in excellent physical condition and there were no physical findings worthy of note. There was slight epigastric tenderness following the taking of food. The urinalysis and blood count were normal. Liver function tests were normal. The gastric analysis revealed a free acid of 10 and a total acidity of 25. The patient had not lost any weight.

A gastro-intestinal series revealed the presence of a bilocular gastric diverticulum situated on the posterior medial aspect of the gastric cardia close to the esophago-gastric junction. There was no evidence of other gastric or duodenal pathology. The gallbladder visualization was normal. Seventy-two hours after the barium meal, the diverticulum still contained barium.

The patient was a graduate nurse and was anxious to have surgical extirpation of the diverticulum, in spite of the fact that it meant a transthoracic operative procedure. At the time of admission, her distress had become so great that she was unable to carry on her usual nursing duties.

On March 13, 1948, the operation was performed under endotracheal ethylene, ether anesthesia. The patient received preoperatively Seconal gr. 1½, morphine sulphate gr. 1/6 and scopolamine gr. 1/150.

The patient was placed supine on the operating table with the left side slightly elevated by a sandbag, producing approximately a 15° elevation from the horizontal. The kidney rest, attached to the table, was placed beneath the patient at approximately the tenth thoracic segment. This was slightly elevated in order to produce a slight degree of hyperextension and left scoliosis of the trunk at this point. The kidney brace was applied to the right side of the table, to prevent the patient from rolling too far over when the table was later tilted.

The incision was begun on the abdomen one inch to the left of the midline and one and one-half inches superior to the umbilicus. The incision was carried in a left superior oblique direction into the eighth interspace, and onto the thoracic wall to about the mid-axillary line. The abdominal cavity was then opened and the costal arch was cut at the eighth interspace. The table was then tilted to the right for about 10°. The incision was extended through the intercostal muscles entering the left pleural cavity.

The diaphragm was incised from the eighth intercostal space of the costal margin toward the esophageal hiatus, for a distance of about half-way. The ribs were held apart by a self-retaining rib retractor and the small intestines and colon were packed off into the lower abdomen. The phrenic nerve was not crushed, as is done when more extensive procedures are performed through an abdomino-thoracic incision.

The stomach was easily delivered into the wound and excellent exposure of the entire greater curvature was obtained. The vessels along the greater curvature of the stomach were clamped, ligated with quilting cotton, and severed. This was begun at about the middle of the greater curvature and continued upward to the esophago-gastric junction. In this way the upper half of the greater curvature was completely free.

Downward traction was then exerted on the stomach and it was possible to rotate it to the right and visualize the upper part of the posterior wall. The diverticulum was located on the posterior wall, close to the lesser curvature, and close to the esophago-gastric junction (Fig. 1). There were many peridiverticular adhesions which were carefully dissected away. The neck of the diverticulum was isolated and found to measure

approximately 1.5 cm. in diameter. The diverticulum at its greatest width measured approximately 3.5 cm.

The neck of the sac was doubly clamped with two large hemostats and the diverticulum removed by means of a scalpel. The wound in the stomach wall was then closed with a continuous over and over suture of atraumatic chromic 000 through all layers

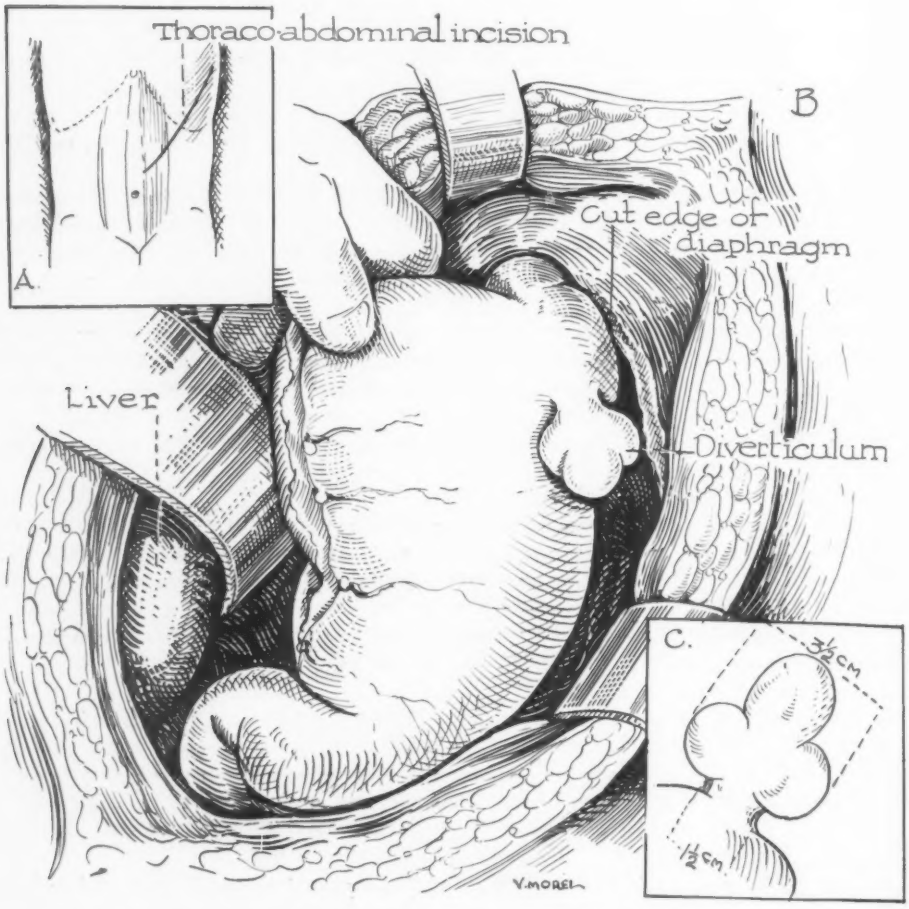

FIG. 1.—Exposure of a tri-locular gastric diverticulum through an abdomino-thoracic incision.

of the stomach. The suture line was reinforced with two layers of interrupted Lembert sutures of quilting cotton, which included the serosa and part of the muscularis. No attempt was made to re-establish the connections between the spleen and the greater curvature of the stomach. The retractors were removed and the wound in the diaphragm was closed with interrupted sutures of quilting cotton reinforced with two interrupted U sutures of No. 8 crochet cotton.

The abdominal component of the incision was closed with interrupted sutures of quilting cotton in the fascia and interrupted sutures of No. 80 cotton in the subcutaneous tissues. The intercostal muscles and pleura were closed together with interrupted sutures of quilting cotton. The suture of the intercostal muscle was made easy by pulling the eighth and

ninth ribs together by means of three interrupted circumcostal sutures of No. 2 chromic catgut, which completely encircled both ribs, care being taken not to include the intercostal nerves or vessels. The costal arch was repaired with interrupted sutures of chromic 0 catgut passed through the costal cartilages on a cutting needle. The subcutaneous tissues of the thoracic component of the incision were closed with interrupted sutures of No. 80 cotton. The skin of the entire incision was closed by means of interrupted Davis sutures of quilting cotton.

A large catheter with suction was left in the thoracic cavity during the closure of the incision and withdrawn only after the insertion of the last skin sutures.

The patient had a relatively uneventful postoperative course except for a moderate degree of intercostal pain. This pain persisted for a period of about six weeks but was relatively slight and did not necessitate the prolonged use of opiates or intercostal nerve block.

The patient was supported during the operative procedure by whole blood transfusions and infusions. The gastric suction was left in place for a period of 72 hours. On the fourth postoperative day she was allowed to take non-residue liquids in unlimited amounts. A soft diet was taken without difficulty on the fifth postoperative day, and a full diet on the eighth postoperative day.

The relief which the patient obtained from the procedure has been complete. She is now able to eat regularly and in normal amounts. There is no discomfort whatsoever following meals regardless of the amount of food taken. At the present time she is performing her full nursing duties as a regular Navy Nurse.

A postoperative gastro-intestinal series on April 28, 1948, (Fig. 4) revealed a shallow filling defect at the site of the diverticulectomy.

Pathologic Report. The specimen consisted of an irregular pouchlike piece of thinned-out stomach wall. It was covered externally by gray fibrous tissue tags. The mucosal surface was divided into three pouchlike projections, each measuring approximately 1.5 cm. in diameter. The entire specimen when laid flat was roughly circular and approximately 3.5 cm. in diameter.

Microscopically, the mucous membrane was normal and a very thin muscular wall was present.

Diagnosis: True gastric diverticulum.

DISCUSSION

A true diverticulum is a rare type of gastric lesion. They are usually located close to the lesser curvature on the posterior wall of the cardiac end of the stomach. At this site the longitudinal muscles are divided into two muscular fasiculi and therefore the mucosa is surrounded only by circular muscle fibers, resulting in an area of congenital weakness.

The diverticula are usually unilocular with a relatively small orifice. The case herein reported is a pathologic rarity in that it was a trilocular diverticulum with a relatively large single orifice (1.5 cm. in diameter). The barium studies visualized only two of the three pouches.

True gastric diverticula rarely measure more than one cm. in diameter. The case herein reported measured approximately 3.5 cm. in its greatest diameter.

Many gastric diverticula produce no symptoms. Those that do produce symptoms can often be treated by a medical regimen consisting of a bland diet, antacids, antispasmodics, and postural drainage. The symptoms usually occur immediately following the taking of food and are undoubtedly the result of the diverticulum becoming distended with food and gastric juices. Evacua-

tion of the diverticulum is delayed because of the kinking which occurs after engorgement and the relatively small size of the opening.

Surgical extirpation is indicated in gastric diverticula whenever the symptoms become severe and are refractive to medical treatment. Furthermore, massive bleeding or evidence of peridiverticulitis with threatened perforation are also indications for surgical intervention. The possibility of any gastric diverticulum being of a secondary nature as the result of a benign gastric ulcer or gastric carcinoma must always be kept in mind, and in such cases surgical interference is indicated.

The most rational surgical approach to gastric diverticula is by means of a transthoracic or combined thoraco-abdominal approach. The surgical removal of these lesions by this means is relatively easy, whereas by the abdominal approach the procedure entails many difficulties.

The case herein reported is noteworthy from several standpoints. The patient was young and the symptoms were of relatively short duration (18 months). The symptoms were of a progressive nature and varied in direct proportion to the amount of food taken at any one time. The patient was almost totally disabled at the time of surgical intervention.

The result obtained by surgical removal of the diverticulum in this case has been excellent. Furthermore, the relative ease with which the diverticulum could be removed by means of the thoraco-abdominal approach suggests that the removal of these lesions can no longer be considered to be a procedure entailing great technical difficulty—as is the case when the abdominal approach is used.

SUMMARY

(1) There are two types of gastric diverticula; true (congenital) and false (acquired). (2) A true gastric diverticulum is a rare type of gastric lesion. (3) The majority of true diverticula occur on the posterior wall of the cardiac end of the stomach close to the lesser curvature at a point of congenital muscle weakness. (4) Gastric diverticula can usually be treated by medical measures. (5) The indications for surgery are as follows: massive hemorrhage, evidence of subacute perforation or secondary ulceration, failure of medical treatment to relieve symptoms, or the possibility of the diverticulum being secondary to gastric ulcer or gastric malignancy. (5) A case is herein reported in which a large trilocular true diverticulum in a young woman was removed through a thoraco-abdominal incision with an excellent postoperative result. (6) The relative ease with which gastric diverticula can be approached by means of a thoracic or thoraco-abdominal incision is emphasized.

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PERFORATION OF THE GALLBLADDER INTO THE FREE PERITONEAL CAVITY WITH SPONTANEOUS HEALING*

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PERFORATION OF THE GALLBLADDER is a rather rare condition. Stone and Douglass[1] reported 17 cases of perforation in a series of 775 gallbladder operations (2 per cent); all 17 perforations were found among the cases of acute cholecystitis (10 per cent). Cowley and Harkins[2] found an incidence of 2.8 per cent of perforations in a series of 12,915 gallbladder operations; the incidence among the acute cases in the series was 13 per cent. Hicken and Coray[3] found an incidence of 25.6 per cent of perforations among cases of acute cholecystitis. Thus, it can be seen that perforations of the gallbladder, though uncommon, are not rare among cases of acute cholecystitis.

The perforation may be: (1) Into the free peritoneal cavity; (2) walled off by adhesions forming a localized abscess; and (3) into another hollow viscus (internal biliary fistula). The last group is the most common, as is well shown by the paper of Wakefield, Vickers, and Walters.[4] These authors reported 176 cases of gallbladder perforation, of which 152 had perforated into the gastro-intestinal tract (cholecystoenteric fistulas), and 24 had ruptured into the abdominal cavity. Only five of the 24 had ruptured and discharged stones into the free peritoneal cavity.

The highest mortality is seen among the perforations into the free peritoneal cavity. Glenn and Moore[5] reported 84 cases of gangrenous cholecystitis, among which were 22 with localized peritonitis and three with free perforations into the peritoneal cavity; two of the three patients with free perforations died, whereas only three of the other 81 patients died.

Here we report an unusual case, found incidentally at autopsy, in which the gallbladder ruptured and spilled calculi into the free peritoneal cavity but went on to heal spontaneously. The patient's past history failed to reveal any episode that might have been associated with the gallbladder perforation.

Case Report. A 67-year-old white male entered the hospital via stretcher in a state of mental confusion which had been present for one day. The history was obtained from a daughter. The patient had had chills, fever, and cough productive of brown sputum, for 3 days. The patient was said to have had a chancre on the penis 13 years before, followed by a positive serology and treatment by hip injections. There was no history of any operations or of any episodes of acute abdominal pain. He had had sore throat, hoarseness, and cough off and on for the past two years and, occasionally, dysphagia.

P. E. Oral temperature was 102° F., respirations 24/minute, pulse 140/minute, and blood pressure 120/60 in the right arm and 118/56 in the left arm. The face was flushed. Lips and nail beds were mildly cyanotic. The left pupil was larger than the right. The

* Submitted for publication July, 1949.

throat was slightly injected. A pulsation was seen and felt in the right supraclavicular region. There was a slight bulging in the second right intercostal space with some increased dullness to both right and left. Tactile fremitus was increased over the right lung field; however, no areas of dullness and no râles were detected. The liver was questionably palpable about 2.0 cm. below the right costal margin. There was no tenderness over the abdomen. No masses were palpable. Patellar reflexes were hypoactive to absent, and Achilles reflexes were absent. The Babinski was positive on the right, negative on the left. The Rhomberg was positive.

Laboratory Findings. A roentgenogram of the chest showed broadening and bulging of the aortic arch; the remaining cardiac shadow was normal. The upper portion of the right lung field showed a rather homogeneous increase in density.

The red blood cell count was 3.58 million. Hemoglobin was 13.0 Gm. The white cell count varied from 12,500 to 13,400 with a persistent shift to the left. Kahn test was negative. Spinal fluid Kahn and Kolmer tests were negative. Blood cultures were negative on

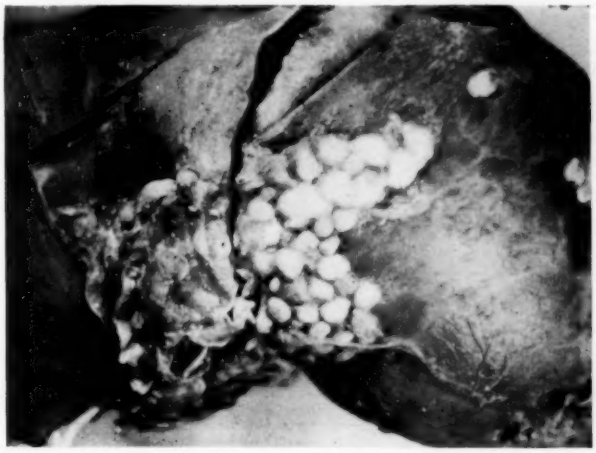

FIG. 1.—Shows the upper surface of the liver posteriorly. Notice the large number of faceted calculi bound to the capsule of the liver.

three occasions. The sputum showed encapsulated gram-positive diplococci on smear and on culture.

Course in Hospital. Because the patient was greatly confused he was placed under restraint. Penicillin, sulfonamides, streptomycin, intravenous fluid, nasal oxygen, and morphine sulfate were given. The temperature remained elevated, fluctuating between 100.5° F. and 104° F. The patient showed no improvement until the seventh post-admission day, when he appeared brighter and co-operative, and generally somewhat better. However, on the eighth post-admission day, he became suddenly worse and died. The clinical diagnoses were: (1) Lobar pneumonia; (2) aortic aneurysm; and (3) tabes dorsalis.

Autopsy Findings. External examination revealed no pertinent abnormality. The pleural cavities contained some bloody fluid, the right about 500 cc., the left about 100 cc. There were numerous pleural adhesions on both sides. The peritoneum was free of adhesions and showed no ascites. There were several faceted stones free in the cavity. These stones were light yellow in color and ranged from 0.3 to 1.0 cm. in greatest diameter. Some of them were in the cul de sac and others were on the under surface of the diaphragm and over the surface of the liver.

The heart weighed 400 Gm., and showed moderate hypertrophy of the left ventricular myocardium; it was otherwise normal. The surface of the aorta was roughened by numerous small plaques. Arising from the arch of the aorta was a large saccular aneurysm, measuring 8.0 cm. in diameter with an ostium measuring about 3.0 cm. in diameter. The aneurysm contained a large laminated clot and was firmly attached to the sternum. Just distal to the arch, and on the descending aorta, there was a second saccular aneurysm 4 cm. in diameter, with an ostium 2 cm. in diameter. This one had eroded quite deeply into the thoracic vertebrae.

The right lung weighed 1200 Gm. The upper lobe was of a dark red color, was quite firm, and did not crepitate. On section it was also dark red, and a bloody fluid could be expressed from the surface. The bronchi contained a small amount of frothy mucous material.

The liver weighed 1800 Gm.; the surface was smooth and brownish-red in color. Loosely attached to the surface there were numerous small, faceted, light-colored stones.

FIG. 2.—Shows the fundus of the gallbladder with the arrow pointing to the star-shaped scar. Several calculi can be seen in the gallbladder fossa, to the left of the gallbladder.

These were found along the gallbladder fossa and over the dome of the liver; there were also a few attached to the undersurface of the diaphragm.

The gallbladder was large and thin-walled, and there were no pericholecystic adhesions. It contained a thin yellow bile and several faceted calculi; these were similar to those found free in the abdomen and those attached to the dome of the liver. In the fundus of the gallbladder there was an area of scarring, with puckering of the mucosa, and a star-shaped scar in the muscularis and serosa. The biliary tree was patent.

The rest of the postmortem examination was irrelevant.

Microscopic study did not add much to the gross findings. The gallbladder did not show any evidence of acute inflammation; it did show much fibrosis in the area of the scar.

The final pathological diagnoses were:

1. Organizing lobar pneumonia; right upper lobe.
2. Syphilitic aortitis and aortic aneurysm.
3. Chronic cholecystitis and cholelithiasis.
4. Healed perforation of the gallbladder with free calculi in the peritoneal cavity.

Chemical examination of the calculi, from both the peritoneal cavity and the gallbladder, revealed a large amount of cholesterol and of bile salts.

DISCUSSION

It is generally accepted that a perforation of the gallbladder into the free peritoneal cavity will prove fatal unless surgically treated. Infection, bile peritonitis, and shock, singly or in combination, are responsible for the almost invariably fatal outcome. This is especially true since we have seen that practically all the cases of perforation of the gallbladder occur in patients with acute cholecystitis.

The only cases of rupture of the gallbladder with apparent spontaneous recovery that we were able to find in the literature were two cases mentioned by Dr. Thomas S. Cullen in the discussion of Edwards, Gerwig, and Guyton's paper.[6] The first case was a 61-year-old female who had had severe right upper quadrant pain 15 years prior to operation; she was operated on with a diagnosis of appendicitis, and dense adhesions were found between the duodenum and the gallbladder. Just outside the gallbladder there were about eight small, faceted stones covered by transparent adhesions. The gallbladder was intact and contained several stones, which were removed, and the gallbladder was drained. The patient made a satisfactory recovery. The second case was a 52-year-old female who had had episodes of right upper quadrant pain, on and off, for 30 years. She had had, occasionally, jaundice and clay-colored stools. Her worst attack occurred three years before operation. At operation, the edge of the gallbladder projected above the edge of the liver, and there was a small pile of gallstones situated on the top of the viscus, but snugly bound down by adhesions. The gallbladder, which was packed full of stones, was removed, and the patient recovered nicely. Apparently both cases were the result of walled off perforation, as shown by the situation of the stones and by the dense adhesions present in the area. No reference to a rupture point or scar is made.

In our case, all the evidence points to a perforation into the free peritoneal cavity, the type that entails the highest mortality. How, then, can we explain that the patient was unaware of this episode, as far as the clinical history is concerned?

We believe it likely that our patient developed a hydrops of the gallbladder prior to the perforation. A calculus impacted in the cystic duct would allow for a marked resorption of bile pigments and bile salts from the gallbladder bile. Now, the rupture of a thin-walled, hydropic gallbladder, would result in a minimal degree of infection, bile peritonitis, and/or shock. The degree of peritonitis in our case, at the time of the gallbladder rupture, must have been minimal since no peritoneal adhesions could be found at the autopsy.

SUMMARY

1. A unique case of perforation of the gallbladder into the free peritoneal cavity, with spontaneous healing, is reported.

2. Many gallstones were found free in the peritoneal cavity, and others were attached to the upper surface of the liver, the under surface of the diaphragm, and the gallbladder fossa.

3. A star-shaped scar was plainly seen in the fundus of the gallbladder.

4. It is believed that the patient developed a hydrops of the gallbladder prior to the perforation. That could explain the "silent" clinical history and also the absence of peritoneal adhesions.

5. The autopsy revealed also a syphilitic aneurysm of the thoracic aorta and an organizing lobar pneumonia of the right upper lobe.

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THE KAPPA DELTA AWARD FOR RESEARCH IN ORTHOPEDIC SURGERY

A prize of $1000, donated by the Kappa Delta Sorority, is awarded annually by the American Academy of Orthopaedic Surgeons for the best research done in orthopedic surgery or a related scientific field by an individual in the United States. The second award, for the year 1950, will be presented at the eighteenth annual convention of the Academy in Chicago, January 31, 1951. Researchers interested in competing for this prize are requested to secure further information from Dr. R. Beverly Raney, Duke Hospital, Durham, North Carolina, Chairman of the Award Committee for 1950.

CYSTIC LYMPHANGIOMATA OF THE GREATER OMENTUM*

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CYSTIC LYMPHANGIOMATA of the greater omentum continue to be surgical and pathologic rarities, although isolated instances of this condition have been reported. Variation and confusion in classification and etiology exist in the literature.

The purpose of this report is to add another to those already published. The case described herein offers details in history and physical findings differing from those heretofore reported. A supplementary survey of the literature as a sequel to the reviews by Montgomery and Wolman[28] and by Horgan,[21] both in 1935, is included. Fourteen additional cases are found to have been reported from 1935 up to the present.

CASE REPORT

T. B., No. 81328, female, married, age 45 was admitted on February 7, 1941, with the complaint of epigastric and right upper abdominal discomfort for the preceding 2 months. This discomfort, which occurred after meals or when she lay on her right side, was aggravated by walking or trunk motions. There was no real abdominal pain, nausea, vomiting, disturbance in bowel habits, weight loss or weakness.

Previous History. In January, 1940, the patient had been confined to the hospital because of menorrhagia, metrorrhagia and a progressive increase in the size of her lower abdomen during the preceding year. Menopausal symptoms had appeared 2 years before. Examination had disclosed an enlarged uterus the size of a three and a half-month gestation, which was diagnosed clinically as a fibromyoma. There were no abdominal complaints. No other abnormal physical findings were noted at that time. The condition was treated by uterine curettage and intrauterine application of radium. The pathologic report of the curettings was "congested endometrium in the premenstrual phase." She had remained in good health until the onset of the present complaints. The family history and the remainder of the past personal history were non-contributory.

Physical Examination. The patient appeared well nourished and not acutely or chronically ill. The blood pressure, temperature, pulse and respirations were normal. The thyroid gland presented a moderate degree of soft diffuse enlargement. The abdomen was moderately obese. At and to the right of the umbilicus there was an irregular tender intra-abdominal mass about the size of a grapefruit which could be moved freely from side to side but did not move with respiration. Vaginal examination disclosed a uterus enlarged to 4 times the normal size and which had no apparent connection with the above-mentioned mass. The urinalysis and blood count were normal.

Two gastro-intestinal series failed to reveal any abnormality. The appendix which visualized was fairly large in size and contained a small enterolith. An intravenous urogram was normal except for a slight dilatation of the pelvis of the right kidney and a localized dilatation of the right ureter at the level of the transverse process of the fifth lumbar vertebra.

Diagnosis. In view of the negative roentgen ray findings a definite diagnosis could not be made. The possibility of a mesenteric or omental cyst was considered. The diag-

* Submitted for publication August, 1949.

nosis of an intraperitoneal abscess due to a perforated appendix or carcinoma was entertained.

Operation. (February 18, 1941) Gas-Oxygen-Ether Anesthesia. Right lower muscle splitting incision.

TABLE I.—*Cases Collected from the Literature 1935–1949*

Author	Date	Age	Sex	Character of the Cyst	Pertinent Features
1. Fèvre and Bertrand	1936	3 yrs.	F	Unilocular serous 14 cm. in diameter	Three week history of diarrhea and abdominal pain preceding the appearance of the intra-abdominal mass.
2. Masmonteil, de Parades and Vautier	1939	5 yrs.	M	Multilocular sero-gelatinous	Enlarged abdomen noted soon after birth. Also presented dysarthria, ectopic testicle and hydrocephalus.
3. Dias	1938	3 yrs.	F	Bilocular sero-sanguinous	Exact preoperative diagnosis made.
4. Berger and Rothenberg	1939	1–10 yrs.	?	Not stated	Not described in detail.
5. Berger and Rothenberg	1939	1–10 yrs.	?	Not stated	Not described in detail.
6. Berger and Rothenberg	1939	1–10 yrs.	?	Not stated	Not described in detail.
7. Hall	1940	3 yrs.	F	Unilocular Serous Pedunculated cyst occupying the entire abdomen	Progressive enlargement of the abdomen for three months, with pain, vomiting and dyspnea. Dilatation of the abdominal veins and flattening of the umbilicus.
8. Mills	1941	47 yrs.	F	Multilocular Serous	Incidental finding at repair of an incisional hernia. Cysts also present along antimesenteric border of two feet of ileum.
9. Eichwald	1941	3 wks.	F	Unilocular Hemorrhagic 4 by 5 cm.	Found at necropsy. Death due to small intestinal strangulation from pressure of the cyst.
10. Gray and Sharpe	1941	4 yrs.	F	Multilocular Hemorrhagic 40 by 30 cm. in size	Hgb 34 per cent preoperatively. Five-week history of weakness, anorexia and protuberance of abdomen.
11 Gray and Sharpe	1941	4 yrs.	M	Multilocular Serous 45 cm. in diameter	No cyst detected at appendectomy one year before. No complaints. Prominent thoracic and abdominal veins. Diagnosed as ascites.
12. Hasner	1943	40 yrs.	F	Multilocular Serous	Involvement of greater omentum, mesentery of small intestine and mesenteric part of small intestine.
13 Hurwitt	1943	10 yrs.	F	Unilocular Serous 11.5 by 3.5 by 1 cm.	Clinical features of an acute abdomen due to torsion of the cyst.
14. Coolican	1945	21 yrs.	M	Multilocular Hemorrhagic	Acute abdominal features presumably due to hemorrhage within the cyst.

Findings. The mass occupying the right side of the abdomen was formed by the entire greater omentum, which contained numerous thin-walled cysts of varying sizes. The main portion was made up of a number of large cysts. There were a great number of smaller cysts, some pedunculated and some sessile, scattered throughout the greater omentum. The uterus, enlarged to about 4 times the normal size by fibromyo-

mata, presented a number of smaller cysts on its posterior aspect. The fimbriated ends of both fallopian tubes were covered with clusters of small cysts. There was no involvement of the liver or gastro-intestinal tract, no free fluid and no solid tumor formation. The picture looked like that of an intra-abdominal carcinomatosis.

Procedure. The entire mass was delivered without much difficulty. The entire omentum, together with the contained cysts, was resected up to the transverse colon. The right tube and ovary were removed for pathologic study. Since the lesion appeared benign and because the original symptoms due to the fibroid had disappeared, the uterus and left adnexa which contained similar cysts were not removed.

Postoperative Course. This was uneventful. The wound healed by primary union. Constipation, which had existed for a long time, improved spontaneously.

Pathologic Findings. *Gross.* The specimen consisted of a resected portion of omentum roughly measuring 18 by 12 cm. (Fig. 1). The omental fat tissue, which was

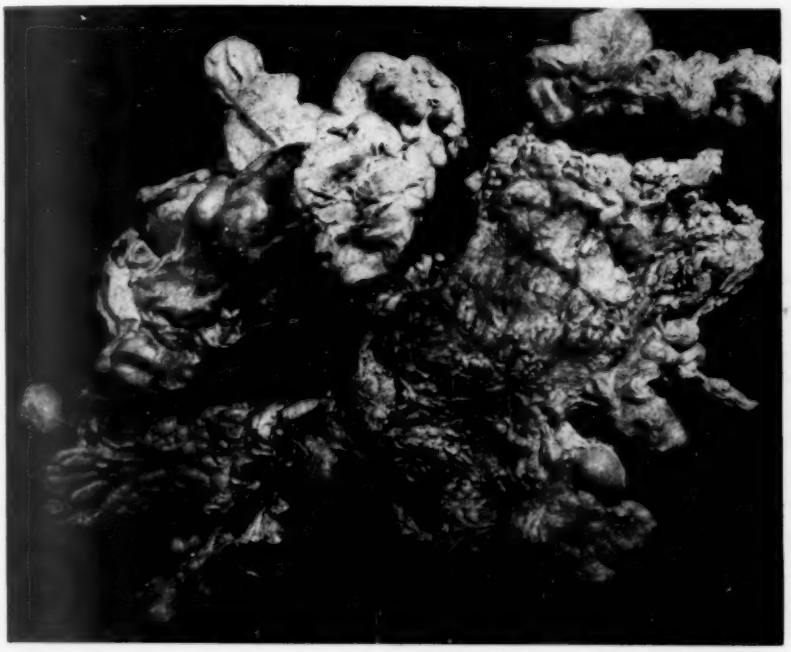

FIG. 1.—Resected greater omentum containing multiple cystic lymphangiomata.

thickened and indurated, contained many translucent cysts too numerous to count. They varied from 1 mm. to 6 cm. in size and occurred singly or in clusters. Most of the cysts, both discrete and clustered, were sessile and were firmly anchored to the omental fat tissue. Attached to the fat tissue at one end of the specimen was a large conglomeration of cysts measuring 15 by 8 by 5 cm., so arranged as to simulate a polycystic kidney. Some of the cysts contained clear serous fluid, whereas the fluid content of others was turbid and more yellowish, apparently due to fatty deposition. A number of cysts presented yellow cholesterol-like deposits within their walls. Those cysts that were opened possessed smooth glistening linings. The resected right tube and ovary were surrounded by clusters of cysts resembling those described in the omentum. The ovary was 3 cm. in diameter, was rather fibrous in consistency and on section presented nothing remarkable.

Microscopic. Sections showed the cysts to have thin fibrous walls lined for the most part with a single layer of flattened endothelial cells. The cystic spaces contained

coagulated albuminous fluid, and in some places foam cell nests and cholesterol crystals as well. Sections of the ovary showed similar cystically dilated spaces on and just beneath the peritoneal surface.

Pathologic Diagnosis. Cystic lymphangiomata of the greater omentum and pelvic peritoneum.

Historical. Although Benevieni described a mesenteric cyst in 1507, the first recorded description of a cyst of the omentum was made by Gairdner[10] in 1852. Since then approximately 115 cases of omental cysts have been reported in the literature. Mesenteric cysts, often classified with those arising from the omentum, have occurred five times as often as the latter. Stillman[33] reported two cases of his own in 1911 plus 19 others collected from the literature. His series included the solitary type of cyst as well as the multilocular lymphangiomata. Montgomery and Wolman[28] reviewed the literature in 1935 and reported two cases of their own plus 53 others which had appeared subsequent to Stillman's article. Horgan,[21] in reporting a case of his own, made an extensive survey of the literature in 1935, and found 97 cases which could be considered as cysts of the omentum. He divided these collected cases into a hematogenous group (48 per cent) and a lymphogenous group (52 per cent).

Incidence. These tumors have been known to occur at any age. The majority have appeared in young people. Montgomery and Wolman found 35 instances in individuals under 11 years and 18 in individuals past 11 years of age. In the series reported by Horgan, 35 per cent were found in the first decade of life and 68 per cent in the first 30 years of life. The youngest case, as reported by Eichwald,[6] three weeks old, the oldest 76 years, and the average 20 years. The condition has been found in many races, the case reported by Dias[4] having been in a Hindu child. The latter writer and Hasbrouck[17] both state that approximately 75 per cent of the cases have occurred in females. Horgan found the ratio of females to males to be three to two. Case histories have not disclosed any familial tendency.

Pathogenesis. Study of the literature discloses considerable inconsistency, with no clearly proved etiologic derivation. The peritoneum itself is rarely the source of new growths. Great similarity in structure exists between the lymphangiomata of the omentum, hygromata of the neck, polycystic kidneys and multiple cysts of the liver. Lymphangiomata have been described involving almost every soft tissue structure in the body.

The common conception, as suggested by Nasse,[30] is that these lesions are congenital in nature. Many observers incline to this source of origin largely because of the more frequent appearance of the condition in the earlier years of life. Hertzler[20] believes that the lesion is laid in a congenital abnormality, but that it is also capable of neoplastic development. Ewing[7] maintains that tumors of the mesentery and omentum are of mesoblastic origin and arise from the tissue between the peritoneal leaves or in the retroperitoneal space; also, that these tumors may be solid, such as lipomata, fibromata or sarcomata, or they may be cystic growths of a more complex character; and that from the formation of lymphatic vessels in this region cyst formation would be ex-

pected to occur. Because of the vascularity of the region and because of the looseness of the contiguous structures these cysts sometimes attain large size.

Earlier writers on the subject (Rokitansky,[32] Winiwarter,[39] Killian,[23] and Kostlivy[24]) advance the theory of occlusion and stasis of either the lymph or chyle ducts as the source of lymphangiomata. Anatomical and pathologic findings have never substantiated this contention. Tilger's[35] case, in which lymphectasis was observed about a healed gastric ulcer, is the only one described in which a possible cause of lymphatic obstruction could actually be demonstrated. On the other hand, Guernsey, a present day contemporary, is of the opinion that the dilatation of the lymphatic vessels and the resultant cyst formation is caused by mechanical occlusion of the lymphatics. This he presumes to be the result of inflammation somewhere in the omentum, the easily expansible structure of the omentum being an important factor in the pathogenesis of such lymphangiectases. To refute this theory of mechanical occlusion and stasis there are the abundant anastomoses that exist in the lymphatic system. Furthermore, any obstructive process of sufficient degree to occlude all the lymphatic channels would be readily noted. In most instances there has been a failure to detect any anatomical or pathologic cause for lymph retention. In addition, local tissue edema, which should accompany such lymphatic obstruction, has not been described. Acute or chronic pelvic or intra-abdominal inflammatory disorders, which are so common, have not been shown to be the cause of such lymphedema or cystic dilatation. One could consider the inflammatory lymphocytic reaction and fibrous tissue formation often found associated with the lymphangiomata to be the result of local tissue reaction to irritation or pressure by the lymph cysts.

Winiwarter, Killian and others have attempted to account for these cysts on the assumption of an obstruction of the thoracic duct. This has never been proved to be the case. Hertzler's experiments showed that all that could be accomplished by ligation of the thoracic duct was the production of a peritoneal exudate.

The majority of recent writers on the subject hold the opinion that the lesion is essentially an embryonic or a neoplastic one, the result of proliferation of the cellular elements of the cyst wall, with secondary secretion of the cyst contents. Grausman and Jaffe[13] consider the process to be a true blastoma arising from retroperitoneal connective tissue and capable of producing such lymphatic channels and lymph cysts by proliferation of the lymphoblasts; that the pre-existing omental lymphatics are not the source of origin; that if these lymphatic channels do become involved it is secondary to their obstruction; and that any proliferative changes in the walls of these lymphatics is due to such obstruction. Montgomery and Wolman are of the opinion that morphologically these lymphangiomata arise from lymph vessels rather than from epithelial embryonic rests, misplaced peritoneal inclusions, blood vessels or degenerated lymph nodes, as has been suggested by various other writers. The occurrence of the lesion in a three-week-old infant, as reported by Eichwald,

favors the theory of congenital and/or neoplastic origin rather than the hypothesis of lymphatic obstruction.

In the patient presented in this report no clinical evidence of the lesion had existed at the time of examination and uterine curettage one and one-half years before. A series of roentgen ray treatments to the pelvis for the control of uterine bleeding had been administered. Under these circumstances such treatment might be considered as a possible precipitating cause of the lesion. The absence of any report of a similar occurrence would leave the development of such a lesion following roentgen therapy open to conjecture. It is conceivable that such therapy may have stimulated a lesion already present but not clinically detectable.

Classification. Review of the literature discloses a lack of conformity in classifying this type of lesion. Hertzler states that the peritoneum itself is the source of origin of relatively few primary tumors and that these must be either endotheliomata or fibrous tumors. Tumors of the peritoneum are commonly metastatic. There are many tumors indirectly but closely associated with the peritoneum, the most common of which are the retention and proliferative cysts which usually occur in the layers of the mesentery or omentum. Small adhesion cysts, the result of irritation or inflammation, frequently occur but have no important clinical significance.

Of the various classifications of intraperitoneal cysts the one offered by Hertzler is most suitable. It is presented here with slight modifications.

A. Proliferative (true) Cysts
   1. Cavernous Lymphangiomata
      a. With serous contents
      b. With chylous contents
      c. With bloody contents.
   2. Cystic Endotheliomata
   3. Dermoid Cysts

B. Retention (secondary) Cysts
   1. Blood Cysts (Resulting from hemorrhage).
   2. Adhesion Cysts (Formed by the accumulation of exudate in pockets).
   3. Degeneration Cysts.
   4. Hydropic Cysts.

C. Foreign Body (infective) Cysts.
   1. Echinococcus.
   2. Gas Cysts (Due to bacteria).
   3. Cysticercus Cellulosae.

Pathology. Morphologic variations of the lymphangiomatous cysts of the omentum have been encountered. Grossly the lesion may appear as a well defined unilocular or multilocular cyst, or it may spread out over the entire omentum like a multilocular air cushion. Rarely, the lesion may consist of firm lymphatic and connective tissue, with little or no fluid contents, or it may appear as a fibro-cystic structure in which multiple small cysts are incorporated. Horgan found 67 per cent of his collected cases to be unilocular and the remainder multilocular. Except for their attachment these cysts lie free in the abdominal cavity. Adhesions, when noted, have been to the abdominal wall and to the abdominal and pelvic organs. Occasionally there may be extension on to adjacent viscera. In the case reported herein the uterus and adnexa were involved.

The lesion may vary in size from a pinhead to cysts that occupy the entire abdomen. In the case described by Young[40] eight gallons of fluid were drained from a single omental cyst. The cyst walls may vary considerably in thickness and are composed of fibrous tissue at times interlaced with elastic fibers. Muscular fibers have been described in the larger cysts. The height of the endothelial cells lining the cysts varies indirectly with the intrinsic pressure. At times stratification of the lining cells may be seen. Scattered areas of lymphocytic or leukocytic infiltration are usually present in the cyst wall or the interstitial tissue. Lymph follicles may be observed. The cyst fluid is usually thin and watery but occasionally it may be thick and gelatinous. In appearance the fluid may be serous, bloody or milky.

Distinction between the lymphangiomatous cysts cannot always be made since all the intermediate stages may exist, the most frequent being the hemolymphangiomata where some pockets contain serous and others bloody fluid. The fluid is alkaline in reaction and coagulates on boiling because of the high albumin and globulin content. The sediment usually contains fatty endothelial cells, cholesterol crystals, red blood cells and amorphous material.

The term "chylous cyst" is a generic one denoting a cyst that contains milky fluid. No substantial proof has been offered that chylous lymphangiomata have any connection with the adjacent normal chyle-bearing lymphatics. Marsupialization of chyle cysts has not been followed by drainage of chyle, healing taking place in a short time. Excision of chyle cysts is not followed by an escape of chyle from the cyst bed. The source of such chyle-like fluid is conjectural. It may arise from a chyle-like transudation from a cyst wall abundantly supplied with lymphatics and blood vessels. Volkmann[36] described a chylous cyst which was found in the supraclavicular region. He mentions nine other cases with chyle cysts of the groin and lower extremity. Henschen[19] studied the fat content of lymph fistulas from the lower extremities and found variations closely parallel to those observed in chyle itself, i.e., from 0.6 to 2 per cent during the fasting state up to 47 per cent following a fatty meal.

Clinical Features. Signs and symptoms may be of three varieties.

1. Those which are asymptomatic and are incidentally detected at the time of examination, operation or postmortem.

2. Those which follow a chronic course. These patients may present palpable intra-abdominal tumors or may complain of abdominal pain or digestive disturbances.

3. Those with acute symptoms.

Symptoms produced by the lymphangiomata are usually insidious in onset and are the result of pressure, torsion or traction. In contrast to the mesenteric cysts they are more likely to create discomfort and distress than pain. The location and laxity of the greater omentum permit considerable mobility and distensibility. Should hemorrhage into the cyst occur reactive phenomena are likely to follow and an inflammatory condition may be simulated. Rupture of a cyst may be followed by signs of peritoneal irritation. Dowd, in his review,

found pain a complaint in 86 per cent and emaciation and weakness in 36 per cent. From their study Montgomery and Wolman reported 32 per cent as having pain or distress, 75 per cent as having diffuse abdominal swelling or a palpable mass, and 9 per cent with no symptoms—the cyst having been discovered incidentally at the time of operation.

Diagnosis. Where the tumor is very small no diagnosis is possible. The infrequency with which the condition exists and the irregularity of the clinical features tend to make the diagnosis a difficult one. It is nearly always made at the time of operation. Montgomery and Wolman found the correct preoperative diagnosis to have been made once in 53 instances. The chief physical sign is the presence of a cystic tumor of great mobility. Ovarian cysts with long pedicles may simulate them. Omental cysts tend to exhibit greater mobility toward the diaphragm, and manipulation of the mass does not ordinarily impart motion to the uterus. In the case reported herein upward mobility was lacking because of extension and adherence of the mass to the uterus. For differential diagnosis one must consider tuberculous peritonitis, ovarian cysts not confined to the pelvis, mesenteric and retroperitoneal cysts, splenic enlargement and renal tumors. The diagnosis of necessity may be made by exclusion. The predominance of the lesion in the early years of life, the presence of a movable cystic mass and indefinite symptoms should cause one to suspect the possibility of such a condition.

Primary malignant omental tumors do occur. They are either fibrosarcomas or fibro-lipo-sarcomas. Strauss and Savre, in describing such a case in a one-year-old child, clinically characterize the lesion by its constant pain, ascites, digestive disturbance and compression of the stomach, intestine and inferior vena cava. The suspicion of malignancy should not deter exploration, since Gould reported such a case successfully operated upon.

Treatment. Surgical extirpation is the only treatment for this lesion. Removal is usually simple. When pedunculated, ligature and division of the pedicle suffices. Sessile cysts can be enucleated, the cleavage plane usually being established without difficulty. This is not feasible when the lesion is a multiple one, or when the omentum is transformed into a fibro-cystic mass. Resection of the omentum is then indicated. Rarely, either because of size or location, marsupialization may become necessary. It is highly questionable whether roentgen ray treatment is of value. Such treatment, which had been given to the patient described herein, if not in itself responsible for the lesion, had failed to arrest its growth.

Prognosis. The immediate operative outlook is good. Montgomery and Wolman noted two fatalities in 53 observations. Horgan[21] states that the operative mortality, although indifferently reported in the literature, appears to be about 12 per cent. All the other patients had recovered and the late results confirmed the efficacy of the surgical treatment. In the supplementary series obtained from the literature and presented above there was one death, the case reported by Eichwald[6] where an omental cyst caused fatal ileus in a three-week-old infant, the diagnosis having been established at necropsy.

These growths are essentially benign and do not recur after removal. The patient who is the subject of this case report is alive and well, with no clinical evidence of any recurrence. There are no reported instances of malignancy in all the recorded cases of lymphangiomata of the greater omentum. Cysts of the omentum, mesentery and retroperitoneum show little tendency to recur or undergo malignant degeneration.

Summary. 1. Another case of cystic lymphangiomata of the greater omentum is submitted. A supplementary survey of the literature from 1935 up to the present has been made.

2. Considerable confusion exists as to etiology. It has not been fully determined whether the condition is an embryonic or a developmental one. The lesion commonly is believed to be a benign neoplasm of mesodermal origin.

3. A course of roentgen ray therapy, administered one year before the growth was detected, possibly might be considered as an etiologic agent. In this case the lesion had invaded the pelvic organs. Only one other instance of such extension has been described in the literature.

4. Although predominantly a lesion of the early years of life it may occur at any age. In the case presented the condition did not manifest itself until past middle life.

5. The treatment is surgical and the prognosis is good.

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CHOLECYSTO-CHOLEDOCHAL FISTULA

AN UNUSUAL FORM OF INTERNAL BILIARY FISTULA*

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INTERNAL BILIARY FISTULA is an interesting and not uncommon complication of chronic disease of the biliary tract. Such fistulas usually occur between organs in close apposition to the biliary system, but Dean[1] has recorded sites of previously reported internal biliary fistulas which indicate that communication with practically any of the abdominal or thoracic viscera is possible. In reviewing the literature, we have been unable to find reports of a pathologic anastomosis between two adjacent structures of the biliary system, namely, the gallbladder and the common bile duct. It seems inconceivable that such communications have not been observed by others. It is possible, however, that their surgical significance has been overlooked. Cholecysto-choledochal fistula implies an encroachment on the common bile duct, which if not recognized, may result in postoperative stricture or division of the duct.

The surgery of the biliary tract may be complicated by congenital anomalies of the ductal system and the vascular supply of the liver and gallbladder. These congenital anomalies have been described by Moses Behrend,[2] Eisendrath,[3] and Flint.[4] Operation may also be rendered technically difficult by changes occurring as a result of chronic disease of the gallbladder and biliary tract. The literature contains many reports of perforation of the gallbladder and bile ducts causing internal communications with other organs. Judd and Burden[5] reported 153 cases of internal biliary fistula. In 117 of these cases, the fistula was between the gallbladder and the duodenum; in four, between the duodenum and the colon; in six, between the gallbladder and the stomach; and in 26, between the gallbladder and the colon. Gray and Sharpe[6] have reported an instance of cholecystogastroduodenal cutaneous biliary fistula. In ten cases reported by Garland and Brown,[7] there were two choledochoduodenal fistulas, five cholecystoduodenal fistulas, one cholecystoduodenocolic fistula, and one cholecystoduodenal abdominal cutaneous fistula. Dean,[1] Eliason and Stevens,[8] Minty[9] and others, have reported various types of internal biliary fistulas. Reviewing the literature, it would appear that the most common fistulas are those between the biliary system and the duodenum. This is probably so because of the close proximity of the gallbladder to the duodenum and the ability of the duodenum to be drawn toward the gallbladder by inflammatory adhesions. It is, therefore, difficult to understand why organs in such close apposition as the gallbladder and common bile duct

* Submitted for publication September, 1949.

should not have been more frequently reported as a site for fistula formation. The reason may lie in the fixed position of the common bile duct and the relative immobility of the gallbladder.

SYMPTOMS

Internal biliary fistulas usually occur in individuals past 50 years of age. Women outnumber men in the ratio of three to one, which is approximately the ratio of chronic gallbladder disease in women to men. In most cases, there is a history of long continued biliary tract disease. According to Dean, the average duration of gallbladder disease prior to operation for internal biliary fistula is 12 years. The patients usually have a history of gallbladder colic, pain, fever, dyspepsia, nausea, vomiting, food intolerance, and jaundice. In short, the symptoms of chronic internal biliary fistula are indistinguishable from those of chronic gallbladder disease. It has been reported that the symptoms of gallbladder disease have been relieved with fistula formation, but this is not the usual sequel. Fistula may be surmised by the presence of gallstones in the vomitus or feces. The first indication that an internal biliary fistula has formed may be the onset of acute small intestinal obstruction caused by blocking of the bowel lumen by stone.

ETIOLOGY

Internal biliary fistulas usually occur as a result of long continued disease of the biliary tract. Repeated attacks of an acute inflammatory nature in the biliary tract produce tissue reaction and thickening of the structures in this area. When a stone becomes impacted in the wall of the gallbladder, the mucosa is destroyed as a result of pressure necrosis, acute inflammation, or both. The individual attack of acute disease may subside, but with succeeding attacks, the walls of the gallbladder and adjacent structures become agglutinated by adhesions. In time, as the pathologic condition becomes more chronic, erosion of a stone through the wall of the gallbladder and an adjacent organ may occur.

The pathogenesis of fistulas between the gallbladder and the common bile duct is similar to that described above. In the three cases which we are to report, the cystic duct was either obliterated by chronic disease or was thick-walled and had a narrow lumen. In two cases, no trace of the cystic duct could be found despite meticulous dissection. It is quite probable that obliteration of the cystic duct plays an important part in the formation of a fistula between the gallbladder and the common bile duct. The contents, both liquid and solid, exert pressure on the gallbladder wall, and this doubtless promotes fistula formation.

CASE REPORTS

Case 1.—The patient, a 53-year-old housewife, was admitted to the Jewish Hospital on September 15, 1947, with the chief complaint of vomiting and abdominal pain. She was said to have developed intolerance to fried and fatty foods 2 years prior to admis-

sion. Such foods caused occasional attacks of epigastric pain, belching, and occasional nausea and vomiting. The epigastric pain was crampy in character. It radiated through the back to the shoulders. Twenty-four hours before admission, the patient began to have severe epigastric pain radiating to the back, nausea, vomiting, and mild diarrhea. The pain was only slightly relieved by hypodermic injections of morphine sulphate, and severe vomiting continued until admission to the hospital. There was no previous history of jaundice or light colored stools. In the past year, the patient had lost 40 pounds by dieting. Past medical history was non-contributory.

On admission, physical examination revealed a temperature of 100.4°, pulse rate 90 beats per minute, and blood pressure 114/70. The patient was obviously in acute discomfort. The skin and tongue were very dry. There was a slight icteric tint to the sclerae. Examination of the abdomen revealed generalized distention with hypoactive peristalsis. Tenderness was present in the upper abdomen, and in the right upper quadrant, an acutely tender mass was palpable under the costal margin, extending about 3 inches below it.

Laboratory examinations revealed the urine to be positive for bile. The sedimentation rate was 31 mm. in 60 minutes. The blood urea nitrogen was 8 mg. per 100 cc., hemoglobin 13.6 Gm., RBC 5,000,000, and WBC 14,750 with 92 per cent polymorphonuclears.

On the day after admission, the patient was operated upon under spinal anesthesia (Fig. 1). The gallbladder was found to be covered by omental adhesions and firmly adherent to the liver edge. It was very much thickened and acutely inflamed. The structures at the neck of the gallbladder and in the gastrohepatic omentum were very difficult to distinguish because of the great amount of fibrous thickening in this region. The gallbladder was therefore opened from above and its contents were removed. These comprised thick bile and stones. The gallbladder wall was opened down to the region of the ampulla, and on examination from within, a large opening was seen, through which a little bile leaked directly into the gallbladder. This opening was explored with probes and was found to lead directly into the common bile duct.

Following this discovery, a search was made for the cystic duct, but it could not be distinguished from the inflammatory tissue surrounding the base of the gallbladder, despite careful search. The common bile duct and hepatic ducts were probed for stones, but none were found. A T tube was inserted into the common bile duct through the opening seen in the ampulla of the gallbladder, and a portion of the gallbladder wall was used to reconstruct the common bile duct around the T tube. A Penrose drain was inserted into Morison's pouch and both T tube and drain were brought out through the wound. The postoperative course was relatively uneventful. The patient had a brown stool on the day following operation. A cholangiogram made on September 25 showed that the ampulla of Vater was patent. The patient was discharged from the hospital on October 8 and the T tube was left in place, but was constantly clamped. The T tube was removed three months after operation and the wound healed completely a few days later.

Case 2.—The patient, a 64-year-old unmarried woman, was admitted to the Jewish Hospital on April 1, 1949, with the chief complaint of right upper abdominal pain. The patient gave a history of repeated attacks referable to the right upper quadrant of the abdomen for the past 25 years. Two weeks before admission this became very severe, and for the last week had been marked by nausea and vomiting whenever any food or drink were taken. One week before admission it was noticed that the stools had become light and the urine dark. She also noticed her skin getting yellow. Social history and family history were non-contributory. Past medical history was negative, except that she had been treated for rheumatoid arthritis. Blood pressure on admission was 100/60. The skin was yellowish in tinge. The patient was a thin, elderly woman with a moderate amount of pain. The sclerae were icteric. The tongue was furry and dry.

Examination of the abdomen revealed exquisite right upper quadrant tenderness and muscle guarding. Electrocardiogram revealed extra systoles. Otherwise, it was within normal limits.

Laboratory tests showed a sedimentation rate 49 mm. in 60 minutes, hemoglobin 12.5 Gm., RBC 3.75, WBC 13,000, 78 per cent polymorphonuclears, urine normal, prothrom-

FIG. 1

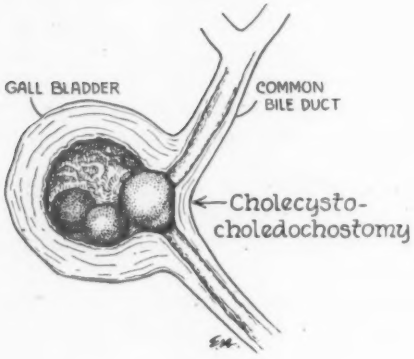
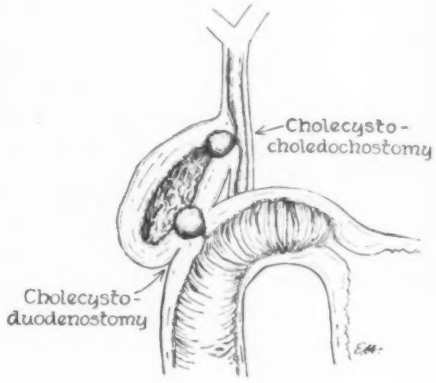


FIG. 2



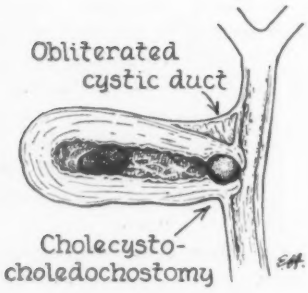


FIG. 3

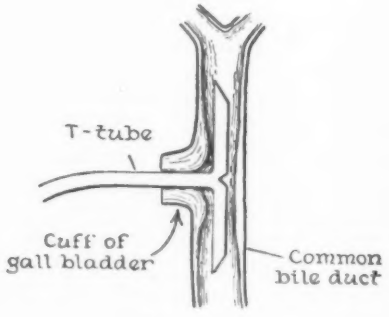


FIG. 4

FIG. 1.—(Case 1) A stone is eroding the thickened gallbladder wall, producing a fistula between the gallbladder and the common bile duct. The cystic duct has been obliterated by chronic inflammation.

FIG. 2.—(Case 2) Separate stones are eroding the gallbladder wall, producing a fistula between the gallbladder and the common bile duct and the gallbladder and the duodenum. The cystic duct has been obliterated by chronic inflammation.

FIG. 3.—(Case 3) A stone has eroded a thickened gallbladder wall to produce a fistula with the common bile duct. A remnant of the cystic duct remains. On microscopic section, this showed obliteration by chronic inflammation.

FIG. 4.—The operative treatment of cholecysto-choledochal fistula. A cuff of gallbladder is preserved to aid in reconstruction of the common bile duct over a T tube.

bin time on admission 50 per cent of normal, blood sugar 102, urea nitrogen 10, van den Bergh 2.1 mg. Operation was performed on April 7, 1949, under spinal anesthesia. On opening the peritoneal cavity, through a right pararectus incision, the gallbladder was found to be completely hidden in adhesions (Fig. 2). The duodenum was closely adjacent and drawn toward the gallbladder by inflammation. The gallbladder was opened

and aspirated. Two stones were removed, each of which were approximately 1 cm. in diameter. Upon removal of one stone, duodenal contents could be compressed through a fistulous opening into the gallbladder. The gallbladder was dissected from above downward and the connective tissue overlying the cystic duct was incised, but no cystic duct was found. The common duct, however, could be readily seen and was not dilated. It was probed and no stones were found in it. The gallbladder was intimately adherent to the common duct and a stone was removed from the point where the ampulla of the gallbladder was in apposition to the common duct. At this point a fistulous tract had developed between the gallbladder and the common duct. The stone was removed. Most of the remaining gallbladder was removed. A T tube was inserted through the fistulous opening and the common duct was reconstructed, using a portion of the gallbladder wall for this purpose. The fistulous tract in the duodenum was closed with interrupted catgut and linen sutures. A Penrose drain and rubber tube drain, in addition to the T tube, were used. The culture of the gallbladder at the time of operation revealed *E. coli*. Cholangiogram performed on April 22, 1949, revealed a patent common bile duct. The dye passed readily through the common bile duct into the duodenum.

Following operation the patient did well. There was considerable bile drainage around the T tube. Because of this fact, and because the cholangiogram previously taken had shown a patent common bile duct and ampulla of Vater, the T tube was removed. Shortly after this, the patient was discharged from the hospital (April 29, 1949). Biliary drainage, which was at first profuse after removal of the T tube, gradually diminished and ceased in 4 weeks.

Case 3.—The patient, a 50-year-old housewife, was admitted to the Jewish Hospital on April 19, 1949, with the chief complaint of jaundice. She had been known to have cholecystitis for 18 months. However, there was a history of pain referable to the right upper quadrant for many years. The present attack began on April 15 with right upper quadrant pain which became worse and was relieved by hypodermics of morphine sulphate. The patient had nausea, but no vomiting was associated with this pain, and she was unable to eat for 2 days. Jaundice was noted on April 18 for the first time. The urine had become noticeably darker since onset of jaundice. Physical examination revealed a jaundiced patient, appearing younger than her stated age, but not acutely ill. Blood pressure 120/80. Physical examination was generally negative, except for voluntary resistance noted in the right upper quadrant of the abdomen. No masses were palpable in this region.

Laboratory examination. Urine normal, hemoglobin 13.4 Gm., RBC 4.40, WBC 9800, with 72 per cent polymorphonuclears, urea nitrogen 13 mg., total protein 7.2, prothrombin time 80 per cent, alkaline phosphatase 4.6, icterus index 15, van den Bergh 1.6 mg. Feces were negative for bile pigment.

One week after admission it was noticed that the jaundice, present on admission, had decreased. The consensus of the medical service reviewing the patient's history and course was that a common duct stone was present. Operation was performed on April 28, 1949, under spinal anesthesia. A right upper pararectus incision was made. The gallbladder was contracted and it contained several stones (Fig. 3). Adhesions between the gallbladder and the duodenum were separated by sharp and blunt dissection. Attempts to define an opening in the gastrohepatic omentum were unsuccessful because of dense inflammatory adhesions. The gallbladder was therefore mobilized from above, but even with this maneuver, it was impossible to define the cystic duct and artery. The gallbladder appeared to be directly joined to the common duct by a fistulous communication. A stone was milked out of this area into the gallbladder. The gallbladder was removed and the common duct and hepatic duct were probed, but no stones could be found. The cystic artery, and what was thought to be obliterated cystic duct, were ligated together. A T tube was sutured into the common duct through the fistulous opening. A portion of the gallbladder was used to facilitate the closure of the common duct. The gallbladder

bed was closed with a chromic catgut mattress suture. A rubber covered gauze drain was placed in the gallbladder fossa. The pathologic diagnosis was "severe chronic cholecystitis, cholelithiasis, adhesion in the cystic duct gallbladder wall with abscess and partial obliteration of the duct, ulceration and perforation of gallbladder wall in the common bile duct." The patient was discharged April 29, 1949, and the tube was removed on June 1, 1949, after a cholangiogram showed no obstruction at the ampulla of Vater.

DISCUSSION

The three cases presented have several features in common.

1. All of the patients had a long pre-existing chronic cholecystitis. The symptoms of gallbladder disease were present for from two to 25 years.

2. Jaundice was a presenting symptom in each case. However, in none of the cases were stones found in the common bile duct itself. Jaundice was probably caused by an acute exacerbation of a chronic cholecystitis complicated by the presence of a stone partially occluding the common bile duct as it eroded through the gallbladder wall.

3. In each case, the artificial communication between the gallbladder and the common bile duct was caused by erosion of a stone. In Case 2, there was, in addition to the cholecystocholedochal fistula, a fistula between the gallbladder and the duodenum, also caused by erosion of a stone through the walls of both structures.

4. In each case, despite meticulous dissection, it was impossible to identify with certainty a cystic duct. The cystic duct seems to have been obliterated by the chronic inflammatory process. Formation of an internal biliary fistula may be encouraged by obliteration of the cystic duct.

5. The surgical implications of this condition should be apparent from reference to the accompanying diagrams (Figs. 1, 2 and 3). It will be noted that extreme caution must be exercised in every case in order to avoid mistaking the common bile duct for a short cystic duct. The cystic duct being absent or obliterated, it is also very easy by making traction on the common bile duct to produce tenting and to injure the duct while removing the gallbladder.

6. Since the gallbladder is intimately fused to the common bile duct by inflammatory adhesions, in order to remove the gallbladder completely, it would be necessary to sacrifice a portion of the wall of the common bile duct. This might result in stricture of the bile duct. For this reason, we have elected to leave a portion of the gallbladder wall attached to the common bile duct and to utilize this portion of the gallbladder wall in reconstruction of the common bile duct around a T tube (Fig. 4).

7. T tube drainage of the common bile duct was used for from two to 12 weeks. Postoperative cholangiograms were made in every case. The T tube was not removed until it was definitely ascertained that bile readily flowed from the common bile duct into the duodenum. In every case, dilatation of the ductal system had returned to normal size at the time of removal of the T tube.

SUMMARY AND CONCLUSIONS

A review of the literature reveals that internal biliary fistulas are relatively common complications of chronic disease of the biliary tract. However, the particular type of internal biliary fistula which we have designated as cholecysto-choledochal fistula appears to be relatively rare. The reasons for this rarity are not well explained. Three cases of cholecysto-choledochal fistula are presented. The etiology and symptoms have been discussed. The importance of such fistulas from the standpoint of the surgeon and the patient have been reviewed.

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BOOK REVIEW

TEXTBOOK OF ANESTHETICS. Minnitt and Gillies, Seventh Edition, May, 1948. Department of Surgery (Anesthesia) The New York Hospital, Cornell University Medical College, New York. The Williams & Wilkins Co., Baltimore, Md.

This is an intelligent survey of the existing anesthetic agents and technics. It presents the basic fundamentals of physiology and pharmacology of anesthetic drugs in a readable and comprehensive style, as well as suitable discussions and recommendations for the administration of these drugs. The section devoted to the choosing of an anesthetic agent is particularly good and the illustrations are excellent.

This book should be of definite value to the medical student and the embryo anesthesiologist who seek a logical and well-organized introduction to the field ot anesthesia.

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PLASMACYTOMA OF THE THYROID GLAND*

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THE OCCURRENCE of solitary or multiple extramedullary plasmacytomas is reported with increasing frequency. Although the great majority of these tumors are found in the upper respiratory tract or in the conjunctiva, the literature contains several reports of plasmacytomas in other situations. In 1943, Hellwig[1] reviewed the literature on this subject and added a case of his own, thus reporting on 128 cases, of which 64 arose in the air passages or in the oral cavity, 47 in the conjunctiva, four in lymph nodes and in other organs, including pleura, mediastinum, spermatic cord, thyroid gland, ovary, gastro-intestinal tract, kidney and skin. Other more recent reports deal with plasmacytoma of the lung,[7] the ileum,[8] the jejunum,[9] and the stomach.[6, 10]

Four plasmacytomas of the thyroid have been reported: one by Voegt[2] in 1938, another by Shaw and Smith[3] in 1940, and two more recently by Hazard and Schildecker.[11] The following case thus brings the total number of reported plasmacytomas of the thyroid gland to five.

Case Report. Mrs. A. MacK., Massachusetts Memorial Hospital No. 314678, was admitted October 1945. The patient was a 77-year-old white, married female who entered the hospital complaining of "swelling of the neck and choking sensations." She had been the victim of arthritis for many years and approximately 10 months before admission she began to notice swelling in her neck and an exacerbation of her arthritis, involving her shoulders. Over the course of the next few months, however, the swelling progressed rather rapidly and 2 months before admission she began to notice choking sensations due to pressure from the swelling. Two weeks before admission she noticed that her voice was becoming hoarse. She gave no history of increasing weakness, fatigue, irritability, emotional instability, appetite increase or intolerance to heat. She had lost 3 pounds in the past year, and had noted shortness of breath only on exertion.

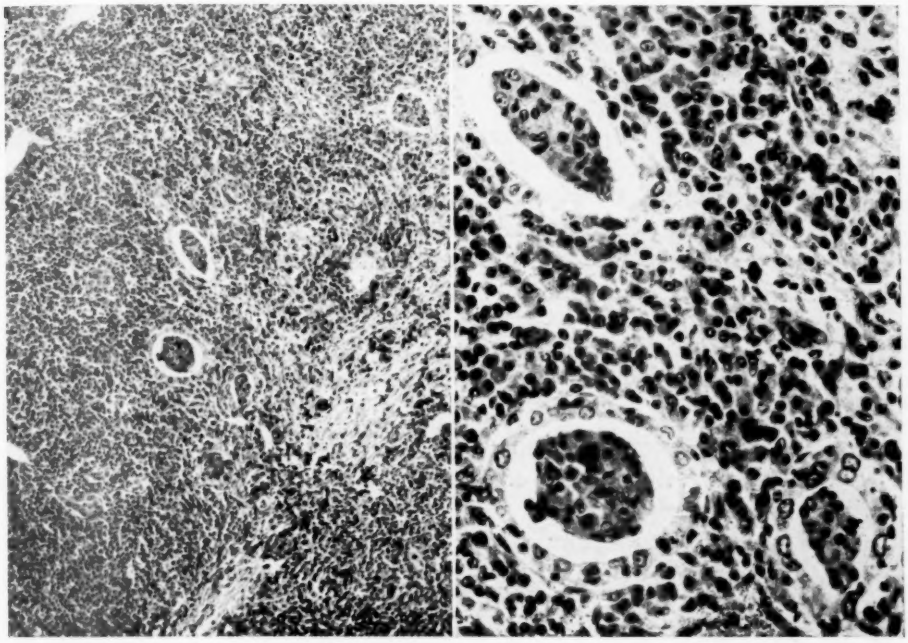
Aside from arthritis of many years duration, fairly frequent attacks of dizziness and tinnitus, and infrequent upper respiratory infections, her system review was unremarkable. She gave no history of severe cardio-respiratory symptoms, and since a cholecystectomy 6 years previously she had had no gastro-intestinal symptoms. She had had 14 uncomplicated, full-term deliveries and had gone through the menopause in her early fifties.

Physical examination revealed a well-developed, well-nourished, elderly, white female who did not appear (acutely or chronically) ill. Positive physical findings were as follows: the thyroid was markedly enlarged with maximum involvement of the upper portion of the right lobe. It was firm and nodular to palpation, easily movable and non-tender. No cervical lymphadenopathy was noted, and there was no exophthalmos, lid lag or tremor of the extremities. A few bilateral moist basal râles were present but no cardiac enlargement was noted. The fingers showed moderate arthritic changes and the radial arteries were sclerotic.

* Submitted for publication September, 1949.

Laboratory studies were all within normal limits. An electrocardiogram was negative. Roentgenogram of the chest and neck showed the trachea to be deviated to the left and backwards, but the heart and lungs were not remarkable. A diagnosis of multiple colloid adenomatous goitre was made.

On October 29, under endotracheal cyclopropane anesthesia a bilateral subtotal resection of the thyroid was performed (F.E.B.). The superior pole of the gland on the right was found to extend high into the neck and the inferior pole on that side extended beneath the capsule, were dark reddish, circumscribed, hemorrhagic areas, measuring 0.2 normal size. The operation was completed without unusual difficulty. The patient's postoperative course was entirely uneventful and she was discharged on her seventh postoperative day.



A B

FIG. 1.—(A) Low and (B) high power views taken from the surgical specimen. Note the marked plasma cell infiltration of the thyroid parenchyma.

Pathologic examination revealed two lobes of thyroid gland, one measuring 10 by 6 by 4 cm. in its greatest diameters and weighing 136 Gm., and the other measuring 5.5 by 4 by 2.5 cm. in its greatest diameters and weighing 40 Gm. On the capsular surfaces were numerous discrete nodules varying in size from 0.4 to 2 cm. in diameter. These nodules had a slightly rubbery consistency. The cut surfaces of the lobes were pale, brownish-grey and glistening. Numerous minute colloid acini, 0.5 to 2 mm. in diameter, were seen throughout the gland substance. Scattered throughout the gland, especially beneath the capsule, were dark reddish, circumscribed, hemorrhagic areas, measuring 0.2 to 1 cm. in diameter.

Microscopic examination showed practically all of the thyroid follicles to be replaced by a massive infiltration of plasma cells among which occasional mitoses were seen and a few giant cell forms noted. The few remaining thyroid acini showed degenerative changes, and their lumina contained desquamated epithelial cells and plasma cells. Several

foci of degeneration, necrosis and hemorrhage were seen, and in some fields there was marked fibrosis with infiltration by both lymphocytes and plasma cells.

Interval Note. In view of the findings on pathologic examination, shortly after her discharge the patient was recalled to the hospital for further study. At this time, roentgen ray studies of the skull, ribs, scapulae, clavicles and pelvis were interpreted as showing no bone pathology. The urine showed no Bence-Jones protein, the NPN was 42 and the total protein was 6.5 Gm. with an A/G ration of 1.3.

Since that time the patient has remained under close observation in Nova Scotia, Canada. In January, 1948, her physician reported her condition to be satisfactory for a person of that age except for her arthritis. At that time, hemoglobin was 70 and the urine showed a trace of albumin, but examination for Bence-Jones protein was negative. Roentgenograms of the skull, chest, spine and lower extremities were negative. No enlarged glands were noted in the neck or elsewhere.

The authors wish to express their gratitude to Dr. G. D. Donaldson, Mahone Bay, Nova Scotia, for the interval report.

DISCUSSION

Since discovery of the plasma cell by Ramon y Cajal in 1890, considerable discussion as to its origin has taken place. In an excellent discussion of this controversy Michels[4] in 1931 summarized the conflicting theories regarding histogenesis of this cell as follows:

1. A histogenic origin from connective tissue cells including tissue lymphocytes, fibroblasts, clasmatocytes, resting wandering cells, adventitial cells and hemohistioblasts.
2. A hematogenic origin from emigrated lymphocytes.
3. A mixed origin from emigrated lymphocytes (monocytes) or preexistent tissue lymphocytes.
4. An origin from immature blood cells (myeloblasts, hemoblasts, erythroblasts, granuloblasts) through aberration or abortion.

More recently, Lowenhaupt,[5] basing her conclusions on studies of autopsy specimens of multiple myeloma, presented evidence supporting the theory that plasma cells arise from tissue histiocytes rather than from lymphocytes.

In 1895, Marshalko published the following morphologic criteria which must be met by a cell if it is to be identified as a plasma cell.[4]

1. Primarily, a specific type of nucleus, small in size, round or oval in contour, with from five to eight distinct, deep staining, angular blocks of chromatin regularly arranged in a circle about the nuclear membrane. (A "clock-face" or "cartwheel" nucleus.)
2. An almost constant, eccentric position of the nucleus.
3. A crescentic juxtanuclear light-staining area due to an accumulation of cytoplasm at the periphery of the cell.
4. A spherical or ovoid cell which, although non-homogenous, is nevertheless devoid of any specific granules.

The specific function of the plasma cell has long been a matter of dispute and is still by no means settled. Satisfactory summaries of the various theories are presented by Michels[4] and by Hellwig.[1]

That plasma cells appear in many types of chronic inflammatory conditions is well known. They are particularly prone to occur where marked infiltration by lymphocytes is seen. Notable among conditions accompanied by an increased infiltration of plasma cells are tuberculosis, syphilis, encephalitis, trachoma, subacute gonococcic infection, chronic endometritis and chronic non-specific cervicitis.

Extramedullary plasma-cell tumors may be either single or multiple, benign or malignant. A relatively small proportion of the 128 cases reported by Hellwig were proved to be malignant. Local invasion and lymph node or bone marrow metastases are cited as evidences of malignancy. Schwander, Estes, and Cooper[6] and Couret[10] have recently reported cases of plasmacytomas of the stomach with local infiltration and regional lymph node involvement. Once bone marrow metastasis is discovered, however, it is difficult to be certain whether the plasmacytoma is the primary tumor or whether it is merely an extramedullary manifestation of a multiple myeloma.

Hellwig[1] concludes that the microscopic appearance does not play a dominating role in predicting the clinical course of a given lesion. He states that "from a prognostic standpoint the localization and the gross appearance seem to be more reliable criteria than the histologic structure. For instance, the plasma cell tumors originating in the conjunctiva have such indistinct neoplastic properties that many writers have regarded them as inflammatory, while tumors of identical cytologic character in the air passages may be highly destructive and may produce widespread metastases."

As regards plasmacytomas of the thyroid gland, there are several points of similarity between the case of Shaw and Smith[3] and ours. Both occurred in females, and the chief presenting symptom in each patient was a "choking sensation." Neither patient showed signs of toxicity, but both were victims of rather severe arthritis. At operation, however, Shaw and Smith noted that the skin was edematous and that the superficial tissues were matted, suggesting an inflammatory process. Also, the thyroid was greyish white, firm to hard, and, on cutting, suggested to them either neoplasm or Riedel's thyroiditis. In our case, on the other hand, there was no suggestion of inflammation or fixation, and the thyroid was rubbery and pinkish-grey on cut surface. At operation, the condition was thought to be a multiple adenomatous colloid goitre. In Voegt's case, quoted by Hellwig,[1] the cut surface of the thyroid was homogenous and brainlike and soft in consistency.

Microscopically the processes in all five cases were similar in that the normal parenchyma was almost completely replaced by plasma cell infiltration. Mitotic figures were described in the cases of Voegt, Shaw and Smith, and in ours. Giant cell forms were described in the two cases of Hazard and Schildecker and in ours. The fibrous stroma in the case of Shaw and Smith and in our case was heavily infiltrated by plasma cells and a scattering of lymphocytes. In one of the cases of Hazard and Schildecker, marked capsular and muscle infiltration was noted.

Shaw and Smith[3] in their conclusion suggest a close relationship between Riedel's chronic thyroiditis and plasmacytoma of the thyroid. They propose that the plasmacytoma in their case, which they believe is of low-grade malignancy, belongs to a type of plasma cell hyperplasia which may occur in conjunction with lymphocytic hyperplasia, the two cellular elements varying in different cases, and, further, that the ultimate course of such a hyperplasia appears to be governed by either local tissue reaction or by cessation of the initial stimuli. They state, "It is thus considered that the changes occurring in our case of plasmacytoma are one aspect (and no doubt a rare one) of the pathologic course of a condition which in itself is uncommon, namely, Riedel's chronic thyroiditis, and that these conditions are expressions of a tissue cell hyperplasia following a physiochemical disturbance that may be dependent on a complex cycle of causes, in part due to disturbance of the neural control and in part of endocrine origin."

This is a difficult theory to refute and certainly the latter phrase, in light of our present knowledge, may possibly be applied to neoplasms at large. It does seem unusual, however, that, if plasmacytoma may be one aspect of the course of Riedel's chronic thyroiditis, it has not happened more frequently in following the course of patients who are known to have Riedel's struma. Certainly in our tissue sections there was nothing to suggest antecedent inflammatory disease of the thyroid. In the first case mentioned by Hazard and Schildecker there was no evidence of precedent thyroid disease, while in their other case there were a few areas in the thyroid suggestive of struma lymphomatosa of Hashimoto. It seems more plausible to consider a plasmacytoma of the thyroid gland a true primary neoplasm rather than an unusual development in the course of a chronic sclerosing condition that characterizes Riedel's chronic thyroiditis.

SUMMARY

1. A case of plasmacytoma of the thyroid is presented.

2. In our opinion, this represents a true primary neoplasm rather than a phase of chronic thyroiditis as has been previously suggested.

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BOOK REVIEW

A Short Practice of Surgery. Hamilton Bailey, F.R.C.S. (Eng.), F.A.C.S., F.I.C.S., F.R.S.E., and R. J. McNeill Love, M.S. (Lond.), F.R.C.S. (Eng.), F.A.C.S., F.I.C.S. Eighth Edition. The Williams and Wilkins Co., Baltimore, 1949.

This textbook of surgery now has gone through eight editions and six reprintings since it was first published in 1932. In this present edition several chapters have been rewritten and a section on peptic ulcer added. There also has been added a considerable number of new illustrations.

In many respects this book well deserves the popularity it has enjoyed. Obviously written for the medical student and the general practitioner, it serves its purpose well. The authors have a simple carefully constructed but easy style which makes for enjoyable reading. They have concentrated an unusual amount of information into one volume and illustrated it accurately. The book is at its best in the objective description of disease and rarely does one encounter a situation in which an important physical sign is omitted. One also is impressed by the sense of balance maintained throughout.

The brevity of the considerations, which acts so well to enhance this volume, also serves at times as a detriment. There is a resultant rigidity frequently noted that could easily lead to false impressions by an indiscriminate reader. An example is seen on page 113 under the discussion of "Lymphangiectasis." "The condition occasionally affects the subcutaneous lymphatics of a limb (Milroy's disease) and amputation may then be required." Again, on page 782 under the discussion of adenoma of the bronchus, there is the statement that "Bronchoscopic examination reveals a tumor which can usually be extirpated without difficulty." There are many thoracic surgeons who certainly would take issue with such a statement. Such use of positive statements in situations where a difference of opinion exists could better be taken care of were modalities given more consideration.

The volume also suffers from a paucity of biochemical and physiologic data relating to surgical disease, and it perhaps is here that one notes its chief difference from current American texts. The authors are at their best in describing acute abdominal catastrophies and lesions of the bones and joints.

Nathan A. Womack, M.D.

CATHETERIZATION OF THE PORTAL VEIN IN MAN FOLLOWING PORTO-CAVAL ANASTOMOSIS

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It is the purpose of this report to describe a method for successful introduction of a cardiac catheter into the portal vein of a patient following the surgical creation of a porto-caval anastomosis.

CASE REPORT

The patient was a 49-year-old alcoholic who had been followed in The New York Hospital for 2 years with a diagnosis of Laennec's cirrhosis. He had had recurrent episodes of melena and of hematemesis over an 18 month period with esophageal varices consistently demonstrable on the esophogram. Despite a persistent glycosuria, his liver function was only moderately impaired; he had never had ascites or edema. On January 19, 1950, a side-to-side portal-caval anastomosis was performed (Dr. Frank Glenn), with immediate reduction of portal vein pressure from a preoperative level of 390 mm. saline to 230 mm. The postoperative course was uneventful and on February 3, 1950, venous catheterization was carried out. Under sterile precautions, a No. 10f cardiac catheter was introduced via the left saphenous vein into the inferior vena cava. It was then manipulated under fluoroscopic control until the tip of the catheter lodged in a position at the level of the twelfth dorsal vertebra and somewhat to the right of the position normally occupied by the inferior vena cava. Further attempts to advance the catheter caused buckling which would not have been anticipated had the catheter tip been free within the inferior vena cava. An injection of 30 cc. of 75 per cent Neo-iopax was made through the catheter and a film of the abdomen exposed at the termination of the injection. This film (Fig. 1) demonstrated opacification of numerous vascular channels which arborized in the region of the liver, joining together into a large trunk which entered the inferior vena cava. A diffuse area of contrast substance was also seen in the mid-epigastrium and was presumed to represent a perenchymal hepatic infiltration. Aside from transient epigastric pain, there were no ill effects following the procedure.

DISCUSSION

To our knowledge, this represents the first reported catheterization of the portal vein in man other than those performed during laparotomy. The procedure in this instance was not difficult and should be reproducible. This report is made in order to draw attention to the method and to emphasize its possible uses.

Portal vein catheterization (only possible in patients in whom an artificial shunt between the portal and peripheral venous systems has been created) has two important, immediate implications. It affords a direct method by which portal vein blood may be investigated in the unanesthetized, "intact"

* This investigation was aided by a grant from The New York Heart Association.
Submitted for publication May, 1950.

patient. Such studies are now in progress and should furnish basic information concerning changes in composition of portal venous blood under a variety of experimental conditions. Secondly, by means of this technic, it is now possible to demonstrate the patency of an anastomosis (although inability to catheterize the portal vein could not be construed as decisive evidence against such patency). This information will be of great assistance in subsequent evaluation of the efficacy of radical surgery for the relief of portal hypertension.

It is believed that catheterization of the inferior vena cava from below rather than through the heart affords better manipulative control of the catheter, but it is recognized that the route to be employed should be indi-

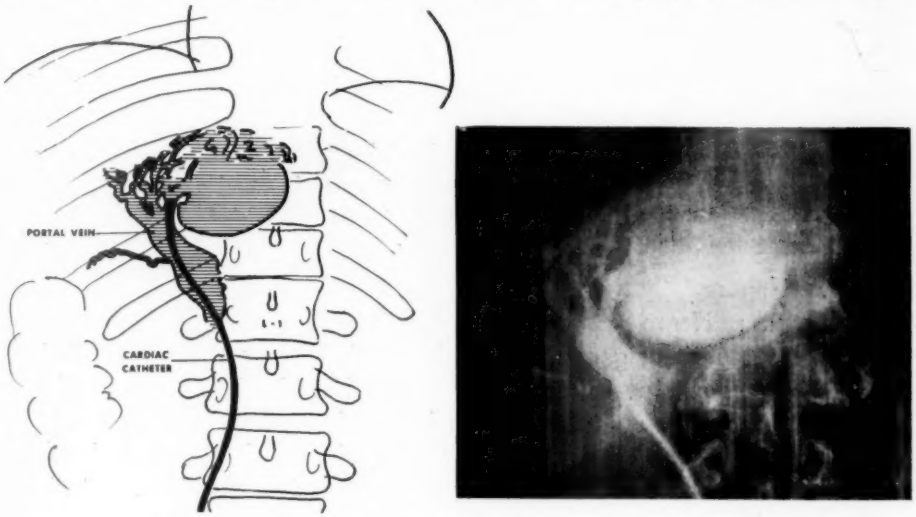

FIG. 1.—Roentgenogram and tracing showing contrast substance injected through catheter outlining the portal vein and some of its intra-hepatic radicals.

vidually planned on the basis of the anatomy of the anastomosis. With this in mind, the site of the shunt is being marked with a metal clip at the time of operation.

SUMMARY

1. Catheterization of the portal vein following porto-caval anastomosis in man has been accomplished and proved by the injection of a radiopaque solution through the catheter.

2. It is planned to utilize this technic in studies of the composition of portal venous blood in man.

AINHUM (DACTYLOLYSIS SPONTANEA)

A REVIEW OF TEN CASES*

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AINHUM HAS BEEN DESCRIBED as a distinct disease by some authors and as a syndrome by others. It is characterized by a constricting band of fibrous tissue which gradually encircles the toe, deepens, and finally strangulates the underlying structures, producing spontaneous amputation. The condition always occurs in the fifth toe of Negroes, and is extremely painful in the later stages.

Although this entity was first described by Clark in 1860, it was not until 1881 that Hornaday reported the first case from the United States. Since that time surprisingly few cases have been reported from this country in comparison to those reported from Africa, Central and South America. Recently Kean and Tucker reviewed 45 cases from Panama—and this a country with a Negro population no larger than some of our Southern States. In 1939 Spinzig carefully reviewed the literature and found that 38 cases have been reported in this country. He added three cases of his own (the largest series to this date) and there have since been reported 12 additional cases. This indicates either that ainhum is a relatively rare occurrence in this country, or that it is not commonly recognized. I believe the latter to be true.

ETIOLOGY

Matas states that the word Ainhum is from the Brazilian Negro patois, meaning "fissure." Da Silva Lima believes the word to be derived from a Nagos expression interpreted "sawing off." These expressions doubtlessly arose from an earlier concept that the condition was caused by constricting cicatrices resulting from cutting the toes with sharp jungle grasses. This theory has been discarded, as the disease has been frequently reported in races customarily wearing shoes. None of Kean and Tucker's cases went barefoot. The similarity of the bone changes in ainhum and leprosy have led some writers to the conclusion that the two processes are related, but the leprosy bacillus has never been demonstrated, either bacteriologically or histologically, from a case of ainhum. Syphilis has similarly been ruled out as an etiologic factor, as has yaws. Trophoneurosis, endocrine dysfunction, and mechanical factors have also been considered. It can only be said that the cause of ainhum is still unknown.

* Submitted for publication September, 1949.

PATHOLOGY

The micropathology of ainhum is limited to the skin and bone of the affected digit. At the site of the constriction, the skin is hyperkeratotic and fibrotic. The bone is entirely absent or shows narrowing of the trabeculae. Unless there is a superimposed infection, there is no evidence of inflammatory reaction. The blood vessels show no thrombosis, thickening, or narrowing of the lumina. The nerves appear normal.

FIG. 1.—This view shows the characteristic picture of ainhum in the later stages.

FIG. 2.—Anteroposterior view of the foot illustrates typical bone absorption as seen in ainhum.

TABLE I

Case Number	Patient	Sex	Age	Duration of Symptoms	Location	Comments
1	B.H.	M	43	6 months	Right 5th toe	Dropped rail on foot
2	M.O.	M	50	10–12 months	Right 5th toe	Repeated minor trauma
3	K.T.	M	61	8 months	Right 5th toe	Stubbed toe
4	J.D.J.	M	44	4-5 months	Left 5th toe	Repeated minor trauma
5	L.S.	F	52	6-8 months	Right 5th toe	Stubbed toe
6	L.C.G.	M	53	3 months 3 months	Bilateral	Occurred first in right 5th toe. Three months later left became involved
7	D.M.S.	M	47	4 months	Left 5th toe	Repeated minor trauma
8	G.L.	F	56	6 months	Left 5th toe	Dropped pail on foot
9	E.W.H.	M	40	10 months	Right 5th toe	Repeated minor trauma
10	J.A.W.	M	45	10–12 months	Right 5th toe	Stubbed toe

SUMMARY OF CASES

I have been able to review the records of ten cases of ainhum occurring in this locality during the past five years. In all of the cases only the fifth toe was involved. In one case there was bilateral involvement. The condition predominated in males; there being eight males and two females. All of the

patients were either in the fourth, fifth, or sixth decade of life. In every instance extreme pain was suffered in the later stages, and it was usually this complaint that brought them to the clinic. A history of trauma associated with the onset of symptoms was always elicited, but such histories were vague, and no great importance could be attached to them. Each of these patients customarily wore shoes, and none gave a history of any familial tendency to the disease.

At some time during the course, each involved toe became infected, requiring several weeks of treatment and inactivity. Pain was always increased by the superimposed infection.

In every case the involved toe was amputated with complete relief of symptoms. There has been no evidence of involvement of the fourth toe after removal of the fifth.

CONCLUSIONS

Ainhum is a disease of unknown etiology involving the fifth toe of Negroes. Since the condition always results in spontaneous amputation and is extremely painful, early amputation is advised. Ainhum is more common in the United States than the literature would lead one to believe.

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Editorial . . .

The Surgical Conscience

"He who through anxiety of conscience busies himself in drawing out the good or evil motives of his manifest actions, who sees vices and virtues at their birth, who follows the insensible progress of culpable thoughts and the secret confirmation of good resolves, who can work the force, nature, and moment of temptations and resistances, holds in his hand almost all the moving strings of humanity, and has only to make them vibrate regularly to draw from them the most powerful harmonies."—Taine.

The moral anarchy of our age sullies man, his institutions, and his professions. The legal profession, the medical profession, even the clergy, all are affected. Negation of conscience torments men of action less than more contemplative individuals. In the medical profession, surgeons are considered men of action. Men of action, without continuous soul searching, may become essentially conscienceless. I propose to consider the surgical conscience in relation to the moral crisis of our time.

Of all the fundamental freedoms of man, none has been more hard won, none now less purely preserved than freedom of conscience. Conscience is the light that guides man's steps to the goal of infinite truths; in its light he examines all actions, approving the right, condemning the wrong. Let conscience be dulled, and falsehood is preferred to truth, irresponsible actions approved.

Each surgeon must master his own conscience. Conscience manifests itself collectively in a well-developed free society, but in this society, the individual conscience must not abrogate its responsibilities. Public and private discussion have sharpened the debate on the moral justification of acts of euthanasia. Conscience will not allow the surgeon to avoid consideration of the moral issue of euthanasia: his aim must be the recovery of the patient. If that cannot be accomplished, it is his moral responsibility not to hasten demise, but by act and deed to allay the fear of death, that "King of Terrors," so that in strength the patient enters with calmness and fortitude that "vast night of forgetfulness."

In our present enthusiasm for the extension of radical surgery for the eradication of cancer, certain moral issues are involved. Thoughtful surgeons question the wisdom of certain ultra-radical procedures. Harvey Stone speaks of "the law of diminishing returns" in surgery as well as in economics. It is not enough to pose the apparently simple question, "Would I submit to such a surgical procedure, to avoid early death?" This question is properly put only to a surgeon of conscience; in some, conscience becomes so dulled as to be insensible or irresponsible. It is not enough for a surgeon to prolong life.

If by his skill life is prolonged only to prove well-nigh unbearable, he may well consider his efforts as fruitless. This is not to deny the merits of ultra-radical surgery for cancer in well-selected individuals, but only suggests the need for careful examination of the moral as well as anatomic bases for certain particularly radical surgical procedures.

I have written in broad terms of conscience as it affects all surgeons. It may be unnecessary to point out the foes of conscience: sloth, indifference, opportunism and avarice, but these defects may prove to be the Achilles' Heel of a surgeon unless correction is applied early in his professional development.

A special group of surgeons comes under scrutiny next: the *teacher and investigator*. Endowed by nature, aided by opportunity and training, selected because of particular abilities and inclinations, these individuals are indispensable for the training of other surgeons and for the orderly scientific progress of surgery. In what particular manner does the surgical conscience determine their actions and decisions? Surgical teaching, unless guided by conscience, can become stereotyped and dogmatic, be based on authority, rather than observation. The *surgical teacher* who cites authority rather than employing his powers of observation shames the intellect of his students. The true surgical teacher arouses interest in observation, thereby awakening the student's mind. "The true Bible to read is nature itself, things as they are, not the printed pages of Galen or another; science comes from observation, not by authority" (Sir Michael Foster). Each new group of students must be taught to see patients through their own eyes. The more students see for themselves the more certain their knowledge. They are then self-taught and therefore more surely taught; their thoughts are their own. Self-education through observation gives reality and permanence to surgical learning. By such a process, the teacher makes surgeons; without it, technicians. Such surgeons become perpetual students, always aware of their shortcomings. The surgical teacher who employs observation as an educational method has a clear conscience.

The *surgical investigator's* conscience must always be sorely troubled. He is not only a teacher, but potentially a creator. The urge of surgical investigators has been a simple (though sublime) dissatisfaction with current methods of treatment, poor records of operative accomplishment and relief or cure, dissatisfaction with things as they are. Such investigators develop because of what Godlee termed "divine discontent," the same divine discontent which led Lister to do his great work, the introduction of the antiseptic method in surgery.

Such discontent is the driving force within every true surgical investigator. Once on the trail of truth he suspects everything in his path. His intuition may be sound but his conscience will not allow him to admit the verity of any printed word until he has subjected it to scrupulous examination. He asks, "Where did this author get his information, from personal observation or the writings of others? If from others, must I check the source?" Having

checked the source, he investigates further into the writer's capabilities, his training, his motives. The surgical investigator never forgets the peculiar human proclivity to admit the power of the printed word.

After appraisal of that already known, the surgical investigator sets forth on his course. His bark is frail, buffeted often by the winds of despair. The rocks on which he may meet disaster are ill-controlled experiments, hastily-drawn conclusions, unconfirmed by adequate observation. Finally, the voyage of search over, certain facts appear established. The writing begins. It is then the surgical conscience must whisper to the author, "Are your observations adequate in number, properly made; are your conclusions properly drawn, have you stated the facts clearly?" If in all conscience the surgical investigator may answer these questions in the affirmative, he can rest soundly.

The closing years of the Age of Reason wrought few changes more important to the development of surgery and the relations of surgeons, one to another, than the creation of the now powerful surgical organizations. The Royal College of Surgeons, Edinburgh, was given its Royal Charter in 1778, that of England in 1800. "Colleges des Chirurgiens" there were earlier in France, but the French "Colleges" never exerted the influence of their Scotch and English counterparts.

What has this historical fact to do with the Surgical Conscience? Simply that with the creation of these institutions, the individual surgeon began to lose his identity and freedom of action. The stage was set and roles created for the *"Surgical Statesmen,"* powerful factors in the leadership and direction of surgical policy. This is not to deny conscience in surgical statesmen but to remind that today surgical thought and progress is dominated in the main by the small surgical societies (Royal Colleges abroad, Associations in America). The leaders of surgical thought today have gained relatively great power, and power can be the malignant force that corrupts reason, that releases man from the beneficent restraint of conscience. Power is the chief enemy of conscience. It is pertinent to recall here Jacob Burckhardt's cogent comment, "Power is of its nature evil, whoever wields it."

The surgical organization, powerful in its leadership, controlling the directional force any progress may take, must ever be mindful of the possible corrupting influence of its power. It must consider the individual surgeon as well as organized surgery. The conscience of surgery in the free society must create and tolerate order, for the continued existence and development of surgery, but it must ever be on guard as to what constitutes proper freedom for the individual surgeon and the surgical profession in its entirety.

Examining and qualifying boards of surgery were created purportedly to safeguard the public against ill- or half-trained surgeons. Considerable progress in this regard already having been made, their initial task completed, such Boards must now consider the welfare of surgery and the individual surgeon, especially the possible stagnation in surgical progress that can result from too vigorous control of the young surgeon in his training years. The fate of the

individual surgeon in organized surgery is no insignificant segment of the ideological battle now dividing the civilized world into two armed camps. To the conscientious surgical statesmen we look for counsel, guidance, and moral leadership in this battle.

A brief consideration has been made of conscience as it affects practising surgeons, surgical teachers and investigators, and Surgical Statesmen, leaders of our profession. In closing, lest the reader conclude this has been written in wholly melancholy pessimism, let him be reminded of those surgeons who by act, word, and deed daily give evidence of the surgical conscience at work. These surgeons of conscience (though perhaps relatively few in number) if left unfettered in our free society, will in time leaven the entire profession. But only a steadfast faith in the ultimate value of individual effort, of the worthiness of the individual surgeon in our over-organized society, will make possible this accomplishment in the moral crisis of our time.

EVERETT IDRIS EVANS.

LIST OF BOOKS RECEIVED

ROWBOTHAM, G. F.	*Acute Injuries of the Head.* The Williams and Wilkins Company, Baltimore, Maryland, 1949.
TERRACOL, J. CORONE, A. GUERRIER, Y.	*La Trompe D'Eustache.* Masson et Co., Editeurs, Paris, France, 1948.
AMERICAN CANCER SOCIETY	*Proceedings of the First National Cancer Conference.* American Cancer Society and the National Cancer Institute of the U. S. Public Health Service Federal Security Agency, New York, New York.
THOMSON, ELIZABETH H.	*Harvey Cushing—Surgeon, Author, Artist.* Henry Schuman, Inc., New York, New York, 1950. (324 pages: $4.00)
VETERANS ADMINISTRATION	*Veterans Administration Technical Bulletins,* Series 10, Volume III, Veterans Administration, Washington, D. C., 1949.
COLLINS, DOUGLAS H.	*The Pathology of Articular and Spinal Diseases.* The Williams & Wilkins Company, Baltimore, Maryland, 1950. (326 pages)
BOYCE, FREDERICK FITZHERBERT	*Acute Appendicitis and Its Complications.* Oxford University Press, New York, New York, 1949. (424 pages; $8.75)

LETTER TO THE EDITOR

Dear Sir:

A reading of the article by Dr. Pulaski and his associates on "Sterilization of the Intestinal Tract by Antibiotics and Supplemental Agents" raises some pertinent questions concerning the place of intestinal "sterilization" in surgery of the colon. The first question to be answered is: "Is it worth-while?" Although it has become almost standard practice to employ some form of chemotherapeutic agent preoperatively for reducing the bacterial flora of the large bowel, it must be conceded that there is no adequate proof that the incidence of complications and morbidity has been significantly influenced by this practice. In fact, some surgeons with the greatest experience in surgery of the large bowel maintain that on the basis of their own experience, the use of these intestinal antiseptics is unnecessary and therefore unjustifiable. During the period since 1940, when sulfaguanidine was first introduced by Poth, there have been many other advances in large bowel surgery, to which might be attributed reduced mortality rates which have unquestionably appeared. Perhaps the same reservations might be expressed as to the role of penicillin and streptomycin administered systemically for the prevention of infectious complications of major surgical procedures. At the Presbyterian Hospital, the operative mortality from all types of operations on the large bowel has diminished from the neighborhood of 15 per cent ten years ago to about 3 per cent during the past two years. However, in attempting to define the reason for this improvement, it is impossible to assign credit to any single change in procedure. It appears that the use of chemotherapeutic agents and antibiotics has probably been of substantial benefit, but I would be hard pressed to prove this point with adequate statistics. Perhaps an even greater contributing factor has been the over-all advances in team-work brought about by full development of the graduate residency training system.

The best evidence for the preoperative use of intestinal antiseptics is not to be found in the clinical literature but rather in the experimental data submitted by Dr. Poth and his associates tending to show a much improved quality of healing of large bowel anastomoses performed in dogs. These preparations showed less edema, less peritoneal infection, and more rapid healing than that in control experiments. This leads to the second question, "Is it reasonable to use intestinal antisepsis?" In other words, "Is it sound professional judgment?" It would certainly seem logical to carry out any procedure which would significantly reduce the bacterial flora of the large bowel and therefore reduce the "dose" of bacteria delivered to the peritoneum with postoperative contamination or by postoperative leakage of a possibly defective suture line. Although the peritoneum can deal with a considerable number of bacteria, there is every reason to minimize this load of contamination, and I believe that Poth's experiments can be cited in further support of this view. The final question is "How is intestinal sterilization best accomplished?" This question is the most difficult one to answer. In the first place, the apparent quantitative reduction in intestinal bacteria seems to depend upon a number of factors in which the bacteriologic technic stands out as being of considerable weight. Differences in diet resulting in differences in fecal composition are of unquestioned importance. The response of a normal bowel may be much greater than that of a bowel containing an ulcerating lesion with varying quantities of mucus. It therefore becomes very difficult to compare the results of different investigators and to come up with a final answer.

Dr. Pulaski and his associates have made a valuable contribution by demonstrating response to oral streptomycin when used with and without adjuvants, such as aluminum pectinate and glucuronolactone. It would be desirable to know how these results compare with those obtained with oral sulfonamides using the same types of cases and bacteriologic technics. His results obtained with polymyxin A are especially

impressive, at least as far as the effect on *E coli* is concerned. Furthermore, one would like to know whether the intestinal bacteria would acquire resistance to polymyxin A as they do to streptomycin. It is this phenomenon which has caused us to discontinue the use of oral streptomycin with and without adjuvants. It might appear better to withhold streptomycin until it is specifically indicated for the treatment of a threatening or established postoperative peritonitis and then to use the drug systemically rather than by mouth. The experimental basis for this attitude has already been reported.

Another drug which seems to offer promising possibilities for intestinal "sterilization" is phthalyl-sulfacetamide. Dr. Edward Howes has been conducting some recent experiments with this drug and has obtained evidence of marked diminution of fecal bacteria particularly in the absence of excessive mucus. Since the problem of acquired sensitivity is not as great with the sulfonamides as it is with the antibiotics, the final outcome of comparative studies will be awaited with interest.

It scarcely needs further emphasis that the results of surgical operations on the colon will depend much more upon the performance of a good anastomosis on a decompressed bowel with a good blood supply than upon any type of chemotherapy which may be administered.

Sincerely yours,

JOHN S. LOCKWOOD, M.D.

EDITORIAL ADDRESS

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